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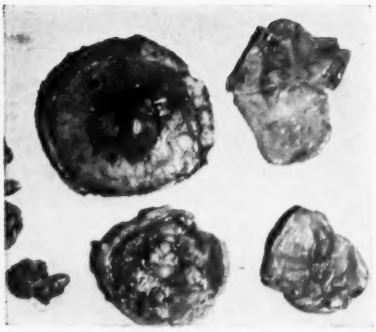

FIG. 1. Case 1. The illustration shows the outer surface of bone and several pieces of tumor removed at the first operation.

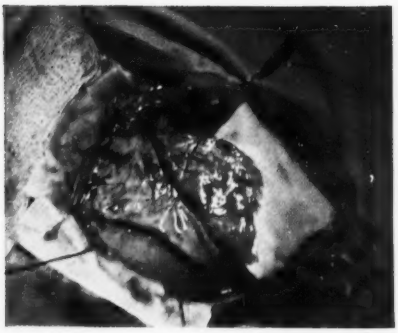

FIG. 2. Case 2. Second operation, showing the inner envelope which contained semi-gelatinous fluid.

FIG. 3. Case 1. Histological appearance of the tumor removed at the first operation. It is a malignant tumor of connective-tissue origin. Notice the formation of collagen fibers among the neoplastic cells. Camera lucida drawing, Mallory's aniline-blue connective-tissue stain×640.

INTRACRANIAL FIBROSARCOMAS OF THE DURA MATER IN CHILDHOOD: PATHOLOGICAL CHARACTERISTICS AND SURGICAL MANAGEMENT

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CONSIDERABLE confusion exists in regard to the classification and clinical behavior of malignant connective-tissue tumors of the dura mater. These neoplasms are infrequent in occurrence, bizarre in clinical behavior, and obscure in histogenesis. Since they are rare, opportunities for study and comparison of different examples are unusual, while the difficulties in establishing the precise site of origin and method of growth make such comparisons desirable. When a patient with one of these dural tumors enters the hospital, there is not sufficient understanding of the lesion to afford an adequate precedent for therapy. For these reasons, we have undertaken a description of three patients with clear-cut fibrosarcomas of the dura mater in childhood. Two of these presented similar clinical syndromes and pathological findings, while the third, histologically identical with the other two, was different in gross appearance, clinical behavior and prognosis.

In making a survey of the literature, it soon became apparent that a precise evaluation and classification of many reported cases would be difficult, owing to the brevity of the descriptions and the changes in conception of the nature of dural tumors since the publications were written. It seemed advisable, therefore, to discuss these tumors in relation to the grouping of tumors arising in the dural connective tissue now in use at this clinic rather than to attempt a discussion and review of all recorded examples.

Among the tumors of the meninges, a sharp distinction should be drawn between the sarcomas of the leptomeninges and the sarcomas of the dura. The sarcomas of the leptomeninges spread freely in the subarachnoid space and from there they extend into the Virchow-Robin spaces. In most instances, the sarcoma lies beneath, and does not penetrate, the arachnoid surface layer. Hence it does not involve the dura primarily and very rarely becomes involved with this structure in the course of its progression.[3,15]

The most frequent tumor occurring in the dura proper is the meningioma. Studies of a series of these tumors[1] have indicated that the meningioma is not of pure fibroblastic origin but is a tumor with stroma. The meningioma arises from arachnoid cells, the source of arachnoid cells in the dura being the Pacchionian granulations. As these arachnoid cells undergo neoplasia, they stimulate a connective-tissue stroma for their support and nutrition. Their habit of growth is thus more like that of carcinoma than sarcoma. Similar conclusions have been reached by others.[9] While the usual meningioma remains localized, certain examples exhibit definite malignant characteristics

(Bailey,[1] Cushing and Eisenhardt,[7] Globus[10] and others). However, malignant meningiomas should be sharply differentiated from malignant dural tumors of purely connective-tissue origin.

When the reports of true sarcomas of the dura are considered, one is faced with the problem of evaluating descriptions in an attempt to determine whether or not "sarcoma," "reticulum cell sarcoma," "round cell sarcoma" and other terms are used for the same type of tumor or for distinct varieties. The three fibrosarcomas on which this report is based are essentially similar in histology to malignant tumors of collagenous connective tissue seen in sites outside the central nervous system. Neoplasms, apparently of this histological type, have been reported by others, in the dura[4,8,16] as well as within the brain substance.[5] While most of the fibrosarcomas of the dura recorded by others arose in the spinal meninges, all three instances in our series were intracranial. The three tumors described in this paper are histologically similar; one was localized and presented very different surgical problems and prognosis from the other two, which were diffuse and saccular in growth. It is unfortunate that we have no autopsy material to determine whether or not there were extracranial metastases. Certainly, there was no clinical evidence of them in any patient. Extracranial metastases from dural fibrosarcomas, however, have been recorded by Caner *et al.*[4] and others.

DIFFUSE, SACCULAR FIBROSARCOMAS OF THE DURA MATER

The two dural fibrosarcomas in this group are almost identical in behavior and in histological characteristics. In both instances there was bilateral involvement of the dura by a diffuse malignant tumor which spread freely in the dura without demonstrable involvement of the underlying brain at any point. Each of these tumors consisted of two envelopes of neoplasm with a fluid-filled sac at the center. When exposed at operation, there was a layer of tumor immediately underlying the bone. In Case 1, the tumor had involved the bone and had extended through it into the inner layers of the scalp. A similar example was recorded by Jaeger,[13] though the tumor described by him was more localized and hence resembled in its dural involvement Case 3 rather than Case 1. On cutting through the layer of tumor beneath the bone, a sac-like cavity was encountered. The inner surface of the sac was formed by another layer of tumor very similar to that forming the outer wall. The underlying arachnoid was smooth and glistening without infiltration by the neoplasm.

The situation and gross appearance of each tumor had many resemblances to a subdural hematoma. In making a diagnostic tap to determine whether or not that lesion was present, the operator might be misled by finding fluid in the precise location that it would be expected to occupy in a subdural hematoma. However, the fluid in both fibrosarcomas of the dura was brown and semigelatinous in character, whereas the fluid of a subdural hematoma is that of changed blood, the cells settling to the bottom, leaving a pigmented, supernatant fluid.[12] All the fluid from the fibrosarcoma re-

mained uniformly dark brown after standing, even for many weeks. One patient (Case 1) came to the hospital with high intracranial pressure and separated cranial sutures. He was comatose at the time of admission. It was apparent that the intracranial pressure would have to be lowered as an emergency procedure before studies could be made. As is always done in our routine procedure in making a ventricular puncture, the needle was withdrawn at the point where the subdural space was apparently reached.[12] It was in this region that brown, semigelatinous fluid was encountered. From this finding, the surgeon recognized that the lesion was not a subdural hematoma. Further evidence of neoplasm was already apparent in the prominence of the parietal bone. In Case 2, the patient on entry had a distinct hydrocephalus and a tentative diagnosis of subdural hematoma had been made by the physician referring the patient to the hospital. In the course of a tap undertaken to determine whether or not a subdural hematoma was present, the same kind of fluid was encountered as in Case 1. Because of this, exploration was carried out through an osteoplastic bone flap, when it became apparent that the dura would have to be sacrificed, and a large dural defect was created. In the closure of these and other similar large dural defects fibrin film made from human fibrinogen and thrombin served to protect the brain and to permit healing without the production of scar tissue.[2,11]

The most outstanding features of the lesions as seen at operation were the diffuse bilateral involvement of the dura, the sac-like structure within the dura with walls of neoplasm continuous with the normal dura at the edges, and the lack of adherence to the underlying arachnoid and brain. From the standpoint of histology, both these tumors were composed of rapidly growing cells of fibrous-tissue origin which produced collagen fibers in varying amounts in different parts of the tumor.

The prognosis in these diffuse, saccular fibrosarcomas of the dura is obviously hopeless. Fibrosarcomas elsewhere are usually radioresistant; little benefit was expected from roentgen therapy. However, roentgen therapy was attempted in Case 1 with an unexpected result; the tumor responded very promptly and favorably to the treatment with disappearance of all symptoms. This excellent immediate result was soon followed by recurrence. Roentgen therapy was not instituted in Case 2 because the patient had had considerable irreversible damage to his brain as a consequence of the hydrocephalus secondary to the tumor. The first patient, however, had no irreparable damage to his brain and might have developed normally if recurrence had not taken place. Since the fibrosarcomas were confined to the dura and did not extend into the brain substance, injury to intracerebral tissues was present only when secondary damage due to increased intracranial pressure had taken place.

Case 1. Increased intracranial pressure from 3 months of age; at 5½ years, asymmetry of head. Exploration—diffuse, saccular tumor of dura. Histology—fibrosarcoma. Temporary improvement with roentgen therapy. Death 3 months after operation.

[*Note:* A brief report of this patient has been published in the JOURNAL OF NEUROSURGERY[11]

in reference to the use of human fibrin foam and thrombin as a hemostatic agent and human fibrin film as a dural substitute. Figs. 5, 6 and 21 to 27 of the earlier paper provide additional illustrations of this patient.]

A.R. (C.H. #278750). A $5\frac{1}{2}$-year-old boy was sent into the hospital in coma. From birth he had vomited a great deal and at 2 months of age weighed only 4 pounds. At 3 months of age the attention of the family physician was called to the fact that his head was increasing in size very rapidly. He noted dilated scalp veins and a bulging fontanelle. For these, he gave medication, the nature of which is not known. At 4 months the patient had two severe falls in rapid succession and following the second he was stuporous for 2 days. His development in

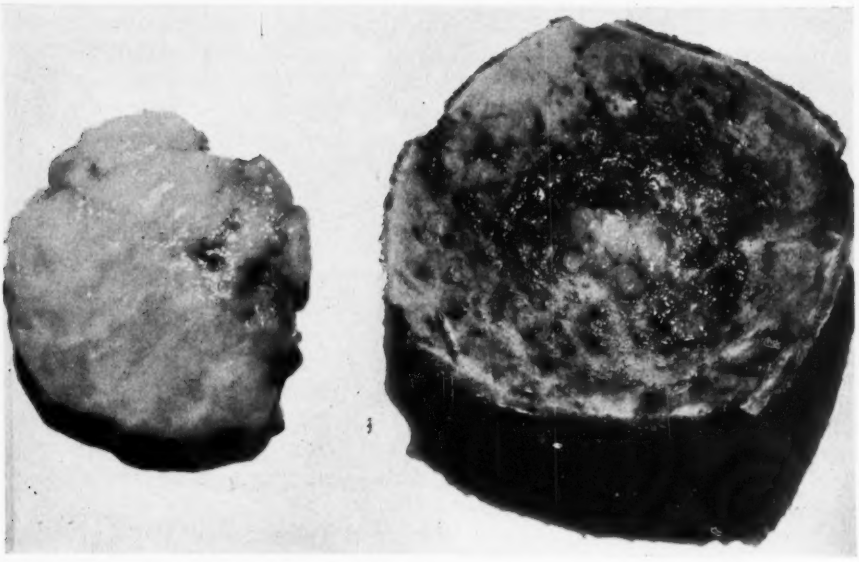

FIG. 4. Case 1. Inner surface of involved parietal bone and plaque of tumor which lay beneath it. These were removed at the first operation.

behavior was very retarded until the age of 3 years when he began to progress fairly well. Two months before admission his parents noticed a distinct change. He refused to eat, slept most of the time, and walked slowly and unsteadily, frequently bumping into objects.

Physical examination at the time of admission showed a fairly well developed, but poorly nourished boy lying on his left side with knees flexed. He could be aroused only by very strong stimulation. The head was abnormally large and in the right parietal region a firm mass the size and shape of half a golf ball was palpable. In the right mastoid region there was a similar but smaller and flatter swelling. The pupils were dilated and discs choked, the neck extremely stiff, and reflexes all hyperactive. Roentgen examination showed separation of the cranial sutures and irregular spotty destruction of the right parietal bone.

A diagnosis of intracranial tumor was made, but because of the patient's extremely poor condition it was decided to lower the intracranial pressure by tapping the right lateral ventricle through the coronal suture. As is customary in this clinic, the stylet was removed as soon as the dura was penetrated, and brown, semigelatinous fluid was recovered. It came freely through the needle and 15 cc. were removed. Following the removal of this fluid the patient's condition improved considerably and the improvement continued as the taps were

repeated during the following six days. At that time a large right temporo-parietal scalp flap was reflected and the bone involved by neoplasm removed (Figs. 1 and 4). Directly beneath this area there was a firm, round, flat tumor mass easily separable from the extensive tumor beneath it. The dura was found to be continuous with a firm flat tumor which separated easily into four layers. The dura and tumor under the bony defect was excised exposing a normal pia arachnoid and cortex beneath. A large amount of the thick fluid previously identified by tapping was removed from the central envelope of the tumor. The cortex was protected with fibrin film and the wound closed. A more extensive exploration was carried out six days later at which time a large bone flap was turned down around the bony defect (Fig. 2). The intra-

FIG. 5. Case 1. Photomicrograph showing the relation of dura and tumor. The dark part in the center is the dura. There is a layer of tumor over the outer surface in the entire field while neoplasm is found on the inner surface only on the right half of the field. Hematoxylin and phloxine stain, ×22.

cranial pressure was again elevated and the cortex was found to have protruded through the defect. The pressure was lowered by the removal of more cyst fluid and all easily available tumor excised. Its gross character was essentially the same throughout the field explored, i.e., it consisted of two huge envelopes one inside the other, the inner one containing large quantities of cyst fluid. This cavity could be seen to extend across the midline anteriorly. In no place was there seen to be any involvement of the arachnoid or of the cerebral cortex. At a later date, a burr hole was made in the left temporal region and the presence of identical tumor demonstrated.

Postoperatively, the patient received roentgen therapy, a total of 2850 r in twenty treatments. Following this, the palpable mass in the right mastoid region disappeared and the patient's condition improved remarkably. After several weeks of good general condition, he started to lose ground and died at home three months after admission to the hospital. (Unfortunately, knowledge of his death reached the hospital too late for any arrangement to be made for autopsy.)

Pathological Findings—Gross. The material submitted for study consisted of several parts. There was a flattened, rounded mass from the dural tumor. This had a diameter of 5.5 cm. and a thickness of 1.5 cm. The outer surface was grayish-pink in color. In most portions it was smooth but here and there it was perforated by soft pale gray tumor. The inner surface of the mass was pale gray and showed an irregular pattern of bluish and yellowish-gray areas. In consistency the tumor was moderately soft. The cut surface was glistening and had a rather gelatinous appearance in which a fine, irregular pattern of yellowish-gray strands could be

FIG. 6. Case 1. General appearance of the tumor in Mallory's phosphotungstic acid-hematoxylin stain. Note the abundance of collagen fibers and the absence of glial elements, ×440.

recognized (Figs. 1 and 4). There were several smaller fragments of dura and tumor tissue varying in size from 1 cm. to 2.5 cm. in diameter. These had the same gross characteristics as the mass previously described.

In addition there was a portion of the skull that was slightly convex, its diameter measuring 8 cm. The outer table was covered with congested periosteum (Fig. 1). From its center protruded a roughly round mass, 3 cm. in diameter, which was raised about 1 cm. above the surrounding bone. It was covered by glistening connective tissue; this was perforated at one point near the border. The tumor in this location varied in consistency from moderately firm to soft. The inner table of the bone showed a very irregular surface roughened by impressions made by blood vessels and other underlying tissue (Fig. 4). In the center, there was an irregular round defect in which the bone was completely missing. This defect measured 1.8 cm. in diameter and was filled with soft tumor masses, pale gray and glistening. The edge of the defect was ragged.

Microscopic. Sections from all portions of the material were stained with eosin-methylene blue, hematoxylin and phloxine, Mallory's phosphotungstic acid-hematoxylin, Mallory's aniline blue connective-tissue stain and Foot's modification of the Bielschowsky-Maresch technic for the demonstration of reticulum. The tumor throughout showed an irregular proliferation of neoplastic cells varying considerably in size and shape. The type cell resembled a fibroblast; it was spindle-shaped and had a clear vesicular oval nucleus usually with several nucleoli (Fig. 6). Mitotic figures were seen in many areas. Collagen fibers were found in large numbers throughout the tissue and these often followed in their course the contours of the tumor cells (Fig. 3). In some areas the cells showed a tendency toward palisading but for the most part there was no regularity of arrangement. Some of the tumor cells were round or polygonal. The cytoplasm stained slightly basophilic and varied in amount. The nuclei were round or oval and very irregular in size. They showed considerable variation in the amount of chromatin. Multinucleated giant cells were present in some fields. While collagen was abundant in all portions of the tumor, it varied considerably in amount in different areas. It was more abundant in those regions where the cells more nearly resembled adult fibroblasts. Fibroglia fibrils were numerous but irregular in arrangement. Portions of the dura persisted in a few places and the relation of the tumor to the dura in these regions is shown in Fig. 5. No glial fibrils or nerve elements were present in any of the sections. Areas of necrosis were seen in many places throughout the tumor. These areas of necrosis were infiltrated with polymorphonuclear leucocytes. Blood vessels were not numerous. They were thin-walled and frequently the walls were invaded by tumor cells. Areas of hemorrhage were present in a few places.

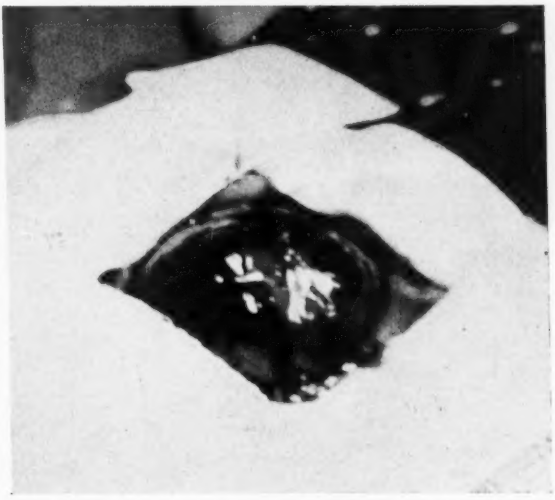

FIG. 7. Case 2. Operative field, which is entirely filled with tumor.

Diagnosis. Fibrosarcoma.

Case 2. Hydrocephalic infant 27 days old admitted with diagnosis of subdural hematoma. Bilateral subdural taps through coronal sutures yielded semigelatinous, brown fluid. Exploration —diffuse saccular tumor of dura. Histology—fibrosarcoma. Patient living but in poor condition 7 months after operation.

H.M. (C.H. #283956). A 27-day-old male infant was referred to the hospital with the diagnosis of subdural hematoma. The birth history was not remarkable. He was considered normal until 11 days of age when he suddenly became deeply cyanotic. The anterior fontanelle was extremely tense and the cerebrospinal fluid pressure measured by lumbar puncture was 300 mm. of water. In the next two weeks his head enlarged 3 cm. in circumference; at that time he entered The Children's Hospital.

On admission, the only positive findings were poor nutrition, enlargement of the head (circumference 16¾ inches) and a tense fontanelle. A lumbar puncture needle was passed into the subdural space on both sides and 10 cc. of brown semigelatinous fluid removed. This fluid

was exactly the same in gross appearance as that removed in Case 1. A small bone flap was turned down in the right parietal region and a similar tumor exposed. It consisted of four layers, the central two enveloping a large quantity of cyst fluid (Fig. 7). No attempt was made to remove more than sufficient tumor for histological study.

The patient was discharged home essentially unchanged. He remains alive but in very poor condition 7 months after operation.

Pathological Findings—Gross. The material submitted to the laboratory consisted of several lobular pieces of soft, glistening, pinkish-tan tissue which together measured 4×2×1 cm. There were several small hemorrhagic foci and in places areas of bright yellow tissue were

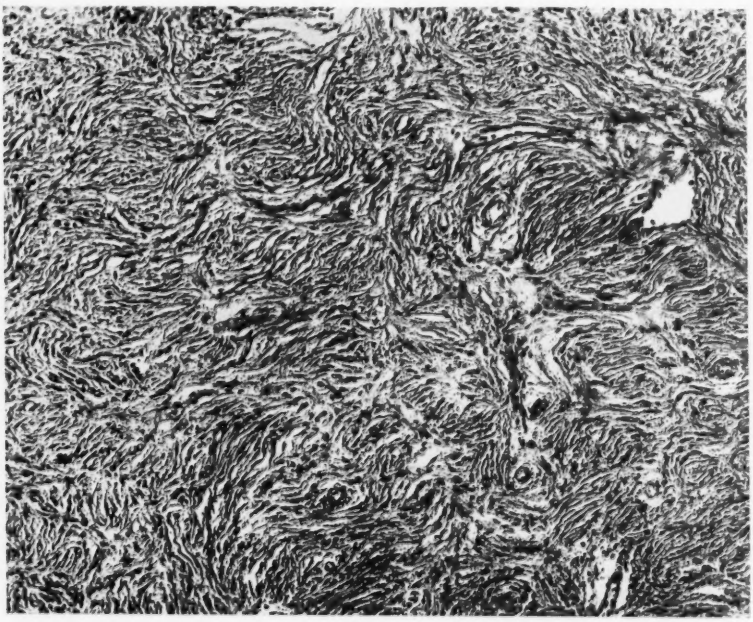

FIG. 8. Case 2. Photomicrograph showing a representative area. Note the irregular growth pattern and the abundance of collagen fibers. Hematoxylin and phloxine stain, ×120.

encountered. No definite architecture could be made out in the gross though a bit of relatively uninvolved dura was attached to one section.

Microscopic. Sections were stained by the same technics as those used in Case 1. These showed very cellular malignant tumor consisting of closely packed spindle-shaped cells. In places these were arranged in whorls but usually they were growing in total disorder. The nuclei showed considerable variation in size and shape from small round structures to large irregular or oval forms. Some were vesicular and most of them presented a well stained chromatin pattern and atypical mitotic figures were seen. The cytoplasm was moderate in amount and sometimes rather poorly defined. The intercellular substance was moderate in amount and varied from delicate fibrils to rather coarse fibers. These followed the contour of the proliferating neoplastic cells (Fig. 8). There were a moderate number of very thin-walled blood vessels. Foci of hemorrhage were encountered in a few areas. A portion of the dura was extensively invaded by the neoplasm. The tumor itself contained no glial elements.

Diagnosis. Fibrosarcoma.

LOCALIZED, SOLID FIBROSARCOMA OF THE DURA MATER

In contrast to the two diffuse saccular fibrosarcomas of the dura, a solid localized fibrosarcoma of the dura was found in a patient entering the hospital because of left hemiplegia and increased intracranial pressure with separation of the cranial sutures. The skull was not invaded by the tumor, localization being made by means of the neurological findings. When an osteoplastic bone flap was turned down a space-occupying lesion was found exactly over the motor area of the right cerebral hemisphere. The tumor was easily dissected away from the motor area much as a meningioma might be separated from the underlying brain. It was found that the area of dural involvement was quite small so that only a small dural defect had to be made. The tumor was removed completely insofar as could be judged at the time of operation and the patient has remained well for a period of six years.

FIG. 9. Case 3. Showing marked separation of cranial sutures, especially the coronal. There are increased convolutional markings and erosion of posterior clinoid processes.

Histologically, the neoplasm was indistinguishable from those of the diffuse type. However, there was no cyst and the localized nature of the lesion made possible its complete eradication by radical surgery. The prognosis, therefore, was quite different from the prognosis of the diffuse saccular fibrosarcomas. In view of the cellular signs of malignancy, however, the long period of survival without recurrence has proved surprising. It indicates that radical extirpation of histologically unfavorable tumors may at times result in complete cure.

Case 3. Markedly increased intracranial pressure and mild left hemiplegia in child of 5½ years. Exploration—solid dural tumor overlying right motor area and adjacent cerebral cortex. Histology—fibrosarcoma. Well 6 years after operation.

F.H. (C.H. #197480). At the age of 2½ years the patient was seen in the orthopedic outpatient department because of forefoot adduction. This was thought to be a mild congenital disorder and light casts were made. In a photograph made at the time of this visit, it is of interest that the left lower extremity was definitely more abnormal than the right. The patient was not seen again until he was 5 years old when he was admitted to the hospital because of weakness of the left hand. In the interim he had been perfectly well and had developed nor-

mally. Two months before entry, his mother noticed that there was difficulty in using his left hand. Shortly afterward some weakness of the left leg was noticed and he complained of headache. Stiffness of the neck and vomiting soon followed.

Physical examination showed a well developed and nourished boy in moderate distress. The deformity of the feet previously noted was still present and his head was unusually large. Percussion elicited a cracked pot sound and there was marked choking of the optic discs. There was weakness of the left shoulder, arm, and leg with increased reflexes throughout on the left side. Ankle clonus was easily elicited on the left and the Babinski response on this side was also positive. Roentgen examination of the skull showed separation of all the sutures,

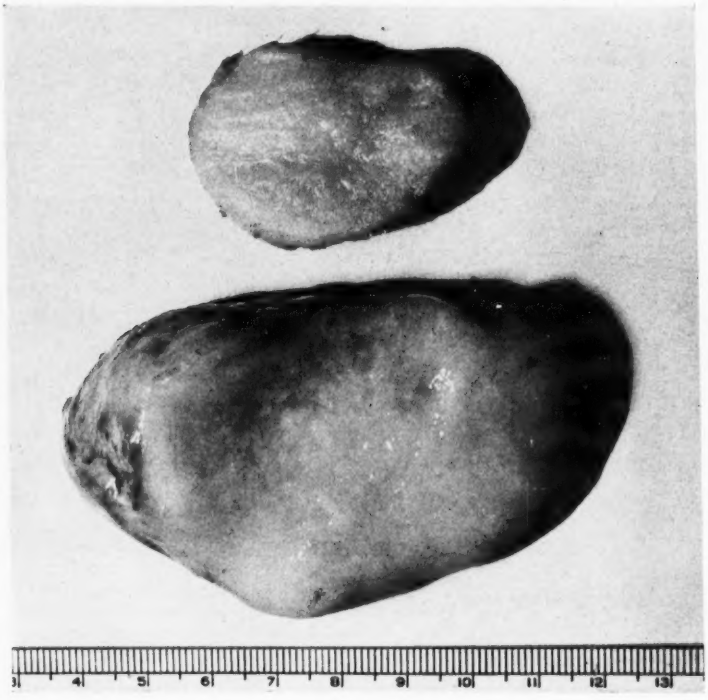

Fig. 10. Case 3. Gross appearance of the major portions of the tumor.

particularly the coronal, and thinning of the posterior clinoids (Fig. 9). Ventriculography revealed dilatation of the entire ventricular system with medial displacement of the right lateral ventricle.

A right bone flap was turned down and a small area of abnormal dura in the mid portion of the field was noted. At this point the dura was slightly yellow and contained a few white flecks. When the dura was reflected it was found that this part of the dura was adherent to a large firm tumor mass overlying the motor cortex. Several large vessels entering the mass were clipped and smaller ones coagulated with the endothermy. There were two clefts in the mass separating it into one large and two small portions (Fig. 10). These were removed separately with the small area of adherent dura. There was no continuity between the tumor and the cortex except by blood vessels. After the mass was removed there was a clear impres-

sion at its site but the arachnoid appeared to be intact. The dural defect was repaired and the wound closed.

The patient did well and was discharged on the eleventh postoperative day. The hemiplegia gradually disappeared and he is now entirely free from symptoms six years after extirpation of the tumor (Fig. 13).

Pathological Findings—Gross. The material as submitted to the laboratory consisted of tumor in three separate pieces. The combined weight of the portions was 90 grams. The largest piece of tissue was roughly kidney-shaped and presented a smooth, glistening, yellow-

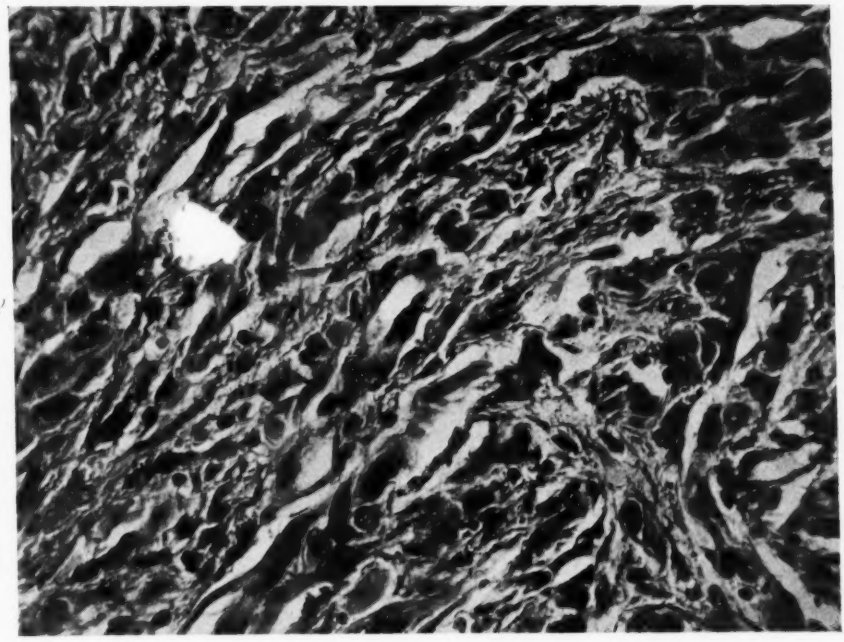

FIG. 11. Case 3. Photomicrograph of the tumor showing the fibroblastic character of the cells and numerous collagen fibers. Note the absence of glial elements. Mallory's phosphotungstic acid-hematoxylin stain, ×460.

ish surface. It measured 7.5×5×4.5 cm. Attached to one surface was an irregular tab of tissue, yellowish-red in color and measuring 4×3 cm., with a thickness of 1 cm. The consistency was firm and resilient while the cut surface everted somewhat at the edges and was yellowish-gray in color. The outer aspect of the tumor mass was whitish-gray, firm and resilient. Throughout the cut surface a fine network of interlacing trabeculations was seen. The second portion of the tumor mass was roughly oval in shape and measured 4.4×3×2 cm. It resembled the first of the neoplasms very closely (Fig. 10). The third portion of tissue was soft and friable in consistency, irregular in outline and measured 3×2×1 cm. It was reddish-brown in color with mottled areas of yellowish-brown.

Microscopic. Sections were stained by the same technics as those used in Case 1. The tumor was composed of cells resembling fibroblasts and intercellular fibrils. The nuclei of the tumor cells were oval and vesicular. They showed evenly distributed chromatin in the form of moderately sized granules. Mitotic figures were occasionally noted. The cytoplasm was moder-

ately abundant and took a slightly bluish stain with the eosin-methylene blue technic. There was considerable variation in size of the cells, some being much larger and containing several nuclei, while others were small, more rounded and had rather scanty cytoplasm. Collagen fibers were numerous (Fig. 11) and an abundant reticular network was illustrated by Foot's

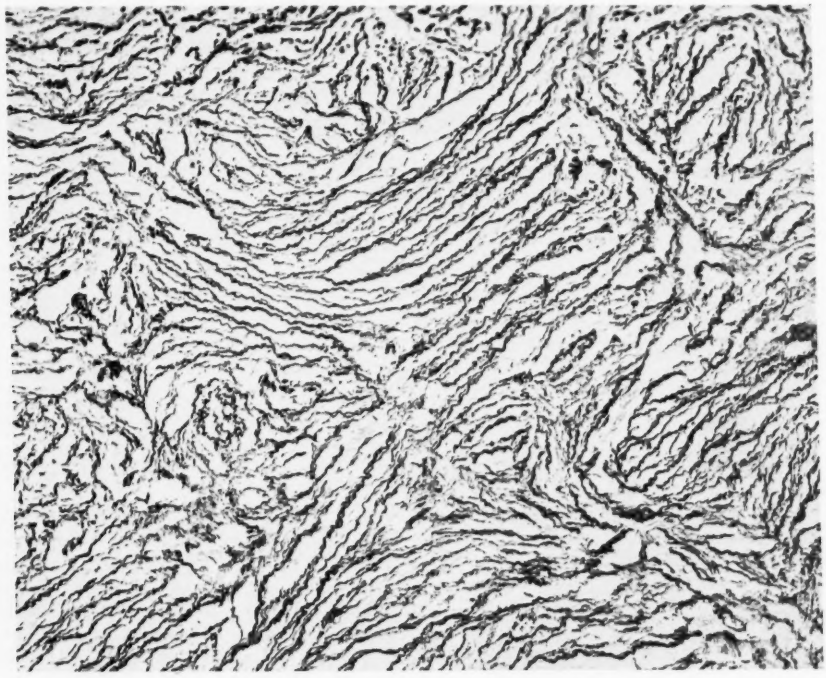

FIG. 12. Case 3. Reticulum stain showing the pattern of the intercellular fibrils. Foot's method, ×106.

technic. Since we regard collagen and reticulum as physically different states of the same substance,[14,17] we consider the abundance of reticulum as further evidence of the fibroblastic origin of the tumor (Fig. 12). The blood vessels were not numerous and were for the most part thin-walled. No areas of hemorrhage were encountered.

Diagnosis. Fibrosarcoma.

COMMENT

The three tumors described in this paper resembled each other very closely in histological appearance. All three consisted of rapidly proliferating cells of fibroblastic type in varying stages of maturity. These cells were laying down collagen fibers. Mitotic figures were present and there was evidence of rapid growth. They correspond, therefore, quite clearly to fibrosarcomas, in whatever connective tissue they arise. From the standpoint of operative findings and gross examination, however, the three tumors fall in two dis-

tinct groups; one group being diffuse and saccular, while the other was solid and localized.

Pathological studies of these tumors indicated that they did not belong to the group of meningiomas and were clearly distinguishable from tumors of arachnoid cells. They also bore little if any resemblance to the small-cell tumors with little or no collagen production that have been described by various authors. It is of special importance in understanding the fibrosarcomas reported in this paper to differentiate them clearly from the sarcomas of the leptomeninges.

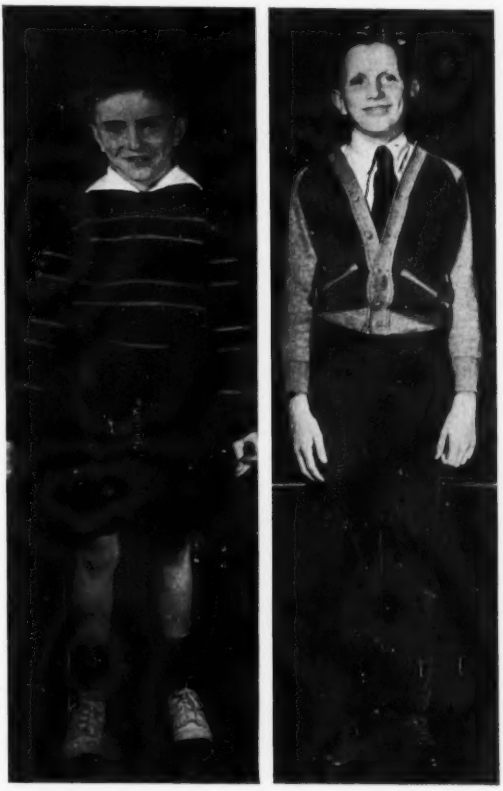

FIG. 13. Case 3. *Left,* Patient 6 months after operation. *Right,* Patient 6 years after operation. At the present time, the patient is entirely free from symptoms.

All three patients were under 5 years of age. We do not regard this as suggesting that such tumors are confined to childhood but the exact counterpart of the diffuse, saccular group has not been found in the large collection of adult intracranial tumors in the files of the Peter Bent Brigham Hospital, though dural fibrosarcomas of the localized solid type have been reported from that hospital by Cushing.[6] Fibrosarcomas in the spinal dura have been reported (Wakeley[16] and others).

Fibrosarcomas of the spinal dura present a clinical syndrome occasioned by a space-occupying lesion compressing the spinal cord. However, the solid localized fibrosarcoma of the cerebral meninges reported in this paper produced its clinical syndrome by increase of the intracranial pressure and localized compression of the underlying cerebral tissue. The diffuse saccular fibrosarcomas resulted in clinical manifestations more like those of subdural hematoma. These resemblances were sufficiently striking for Case 2 to be referred to the hospital with a tentative diagnosis of subdural hematoma. The confusion was less in Case 1 because of the asymmetry of the skull, a finding that pointed directly toward a diagnosis of an invasive neoplasm.

Because of the hopeless prognosis, it might appear that exploration should not be carried out if brown, semigelatinous fluid were obtained in the course of a ventricular tap. However, even with the evidence afforded by the character of the fluid, it would be better to explore all patients suspected of having malignant dural tumors. The exact characteristics of the lesions can then be visualized and too few instances have been studied to permit general conclusions. It is difficult for the surgeon to be sure preoperatively that he is not dealing with a limited, removable tumor containing a cyst. However, such evidence as may be gleaned from this small series would suggest that solid fibrosarcomas of the dura may be localized and favorable for radical extirpation while those of the diffuse saccular type are hopeless. Exploration can do no harm while failure to explore might prevent successful attack on a lesion that could be dealt with surgically. While we have never encountered a cystic teratoma in the same region as these diffuse saccular fibrosarcomas, it is possible that one might take origin at that point. Then a benign lesion of a different histogenesis might be allowed to result fatally if exploration were not carried out when brown, semigelatinous fluid was obtained in the course of a ventricular tap.

The results of roentgen therapy in Case 1 were completely unexpected. There have been very few tumors reported in the literature that are exactly comparable to those of the series here described and have been treated in the same way. For this reason, no very general conclusions can be drawn as to the efficacy of roentgen therapy. In fibrosarcomas of the dura, however, it seems worthwhile trying this form of treatment if the underlying brain is intact. The tumors in our series did not extend into the underlying brain; damage to vital centers and to intelligence were only the result of secondary changes resulting from pressure. The satisfactory immediate response in Case 1 suggests the value of trying any form of therapy that offers promise of combatting the tumor. If the tumor is controlled before irreversible secondary changes have developed in the cerebral tissues, a favorable result may be expected. The underlying brain in Case 2 was damaged because the patient had an expansile skull and did not show signs of increased intracranial pressure until the tumor had caused irreparable damage to the brain itself. No form of therapy could then be expected to restore the patient to complete physical and mental health.

Quite a different situation existed in dealing with the localized solid fibrosarcoma in Case 3. There surgery alone effected a cure with complete regression of neurological findings, and satisfactory growth and intelligence have followed for a period of 6 years.

The study of these three patients with intracranial fibrosarcomas of the dura mater has served to indicate the great variation in method of growth that may take place in tumors of identical histology. Not only does the prognosis in a given tumor depend upon its histology but upon its location and extent.

SUMMARY

Three examples of intracranial fibrosarcoma of the dura in childhood are presented. Two of these were diffuse, saccular neoplasms which were bilateral at the time of operation and were hopeless in prognosis. The third was a localized, solid lesion which did not recur and the patient is symptom-free 6 years after operation.

Fibrosarcomas of the dura should be sharply differentiated from leptomeningeal sarcoma and from invasive meningiomas. These fibrosarcomas of the dura resembled extracranial fibrosarcomas in histology but showed considerable differences in method of growth and progression.

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GIANT CELL TUMOR OF THE SPHENOID BONE REPORT OF A CASE

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GIANT cell tumors of bone are most commonly found in the long bones but occasionally they occur in the skull and elsewhere. According to Wattles[9] the bones affected are, in order of frequency, long bones, small bones, maxilla, mandible, vertebrae, ribs, scapula, clavicle and the ethmoid, sphenoid, temporal and frontal bones. From a search of the records in the surgical pathologic laboratory of the Johns Hopkins Hospital for a period of thirty-five years, Geschickter and Copeland[4] found only 22 cases of giant cell tumor occurring in the skull. Two of these were found in the sphenoid bone and the remainder in the jaws. Details of the two tumors in the sphenoid bone were not given. Analysis of the available medical literature has failed to reveal any other cases of giant cell tumor of the sphenoid bone. This is one of the reasons that the following case is reported.

REPORT OF A CASE

G. G. a 12-year-old girl was seen by me on June 16, 1943 at the Baptist Hospital in New Orleans at the request of Dr. William H. Gillentine. About two weeks before, the child had completed the seventh grade at school at the head of her class. Shortly thereafter she began to vomit and complained of headache and double vision. The child's mother stated that the patient had been irritable for several months and that occasionally there was a one-degree rise in temperature. She had grown three inches in height in the past year and had not begun to menstruate.

FIG. 1. Note destruction of sella turcica. This appearance is identical with that produced by cerebellar tumors of long standing.

Examination. A complete sixth nerve paralysis on the right was noted, the pupils were unusually large and the eyegrounds and visual fields were normal. The remainder of the physical and neurologic findings were negative.

Hematologic examination revealed a red blood cell count of 5,120,000, hemoglobin 97 per cent and white blood cell count of 7,350. Spinal fluid pressure was 140 mm. of spinal fluid. The total protein content was 32.4 mg. per cent. The gold-sol test was 2111100000. The Wassermann reaction was negative.

Roentgenograms of the skull (Fig. 1) revealed complete destruction of the sella turcica suggesting either a cerebellar tumor or a large adenoma of the pituitary gland.

Course. A tentative diagnosis of tumor destroying the sella turcica was made and the patient was discharged from the hospital June 17, 1943 for a period of observation at her home. She began to sleep much of the time during the day, vomited occasionally but experienced no further headaches. The visual fields, which were examined on June 24, 1943, showed central scotoma on the right. Visual acuity on the right was 20/50 and on the left 20/15.

Admission. On June 30, 1943 the patient was admitted to the Touro Infirmary. Two days

FIG. 2. Air in the displaced cisternae chiasmatis and interpeduncularis outlines the superior surface of the tumor.

before numbness of the left cheek had developed and vision in the right eye had begun to fail. An encephalogram made under intravenous anesthesia revealed a normal ventricular system, but a rounded mass was seen in the region of the sella turcica which had elevated the cisternae chiasmatica and interpeduncularis (Fig. 2). The impression was that the patient had an atypical pituitary adenoma, an uncalcified craniopharyngioma or a teratoma of the pituitary region.

Operation I. On July 3, 1943, under local anesthesia, exposure of the optic chiasm revealed that the diaphragma sellae was in contact with the optic nerves and chiasm but it was not sufficiently elevated to flatten the optic nerves or to separate them. The diaphragma was coagulated and the sucker was pushed through it. A large cavity occupied the region of the sella turcica. The fluid contents of the cavity were aspirated by the sucker. A portion of tissue from the tumor adhered to the sucker and this was sent to the pathologist for histologic diagnosis. From the hole in the diaphragma there was brisk, persistent bleeding which was controlled by plugging the hole with a piece of temporal muscle. The dura was closed with cotton and then sutured to the periosteum. The bone flap was laid in place; the scalp was closed in two layers with cotton.

Pathological Report. Dr. J. R. Schenken made a diagnosis of giant cell tumor of bone (Fig. 3). This diagnosis was also made by Dr. Granville Bennett of the Tulane Medical School.

Course. The patient was discharged from the hospital July 17, 1943. Shortly after operation she gradually became completely blind in the right eye and paralysis of the third nerve appeared. Dilation of the left pupil followed.

Light roentgen therapy was then given by Dr. Meyer Teitelbaum: 1800 R to each of three ports, the daily dosage being 300 R alternating between the three fields. This was done by means of a small cone attached to a roentgen-ray machine at a target distance of 70 cm.

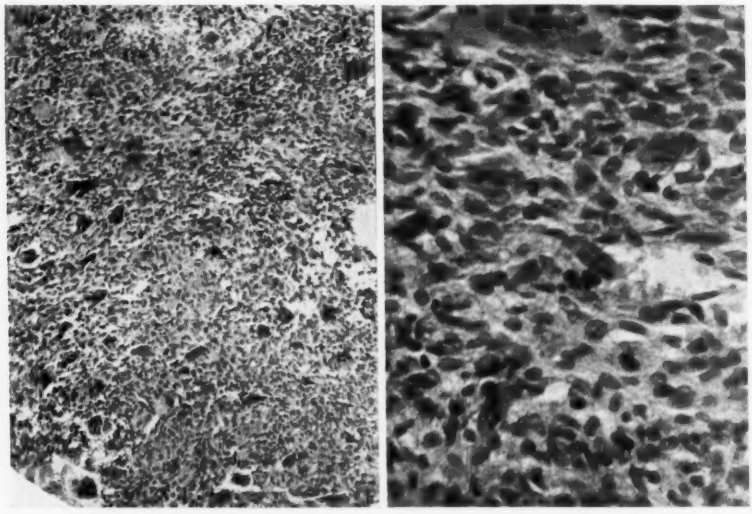

FIG. 3. Low and high power views of the tissue removed from the tumor at the first operation.

About Sept. 15, 1943 vision in the left eye began to fail. The child continued to grow progressively worse. She lost considerable weight and complained of abdominal pain and nausea in addition to headache and numbness of the face. Hypodermic injections of pituitary extract were given for several weeks without improvement in the symptoms.

In September 1943, Dr. George T. Pack and Dr. W. H. Stewart of New York City were consulted by mail. They agreed that the growth presented the microscopic appearance of benign giant cell tumor and suggested heavy doses of irradiation. This was carried out but without apparent effect upon the rate of growth of the tumor.

Roentgenograms of the skull on Jan. 7, 1944 showed a considerable increase in the destruction of the floor of the skull (Fig. 4). Examination with the pharyngoscope on this date showed pronounced bulging of the posterior wall of the nasopharynx. By this time the patient was completely blind but not confined to bed.

As the child continued to get worse, her parents conferred with various surgeons throughout the country regarding her condition.

Operation II. On March 11, 1944 in St. Louis, she was operated on by Dr. Roland M. Klemme. The operative note, which he was kind enough to send to me, is briefly abstracted. Following anesthetization with avertin, 0.5 per cent solution of procaine hydrochloride and a few drops of ether, a rather large unilateral right frontal flap was turned down, part of the previous flap being utilized. Elevation of the brain, extradurally, uncovered an enormous tumor completely filling the floors of the frontal and temporal fossae. With the electrosurgical knife, the tumor was excised from the bone and the entire temporal fossa was emptied as well as most of the frontal fossa along the greater wing of the sphenoid. All bleeding points were

controlled with the electrosurgical knife; little bleeding occurred. It was immediately apparent that the optic nerves and chiasm were completely involved, so the right optic nerve was dissected out in its entirety. The posterior third of the bony orbit of the eye had been completely eroded. All the tumor around the globe of the eye was removed. The incision was then carried forward and the tumor, extending down into the sphenoid and both antra to the soft palate, was excavated. After the optic chiasm and the nerves had been freed, the sheath of the optic nerve was split on the right, and the nerve lay perfectly free and seemed to return to its normal size. The one on the left was so constricted that this procedure had little effect. The balance of the tumor was removed piecemeal and there was a lot of bone in conjunction with the tumor. Erosion of the petrous tip of the temporal bone could be seen on the right side and the same condition appeared to exist on the left. The floor of the temporal fossa was completely eroded and the soft palate could be felt. The posterior third of the bony orbit of each eye had been completely eroded, and the sphenoids and ethmoids were gone. About two-thirds of the clivus was completely eroded and the tumor was removed from this area in its entirety. At the end of the procedure the optic chiasm and both optic nerves hung suspended in mid air unsupported from the base of the brain to the globes of each eye. The patient's condition at the end of the operation was excellent. The blood pressure was 120/85, pulse around 90 and respirations were normal.

FIG. 4. Note destruction of floor of skull including apices of petrous pyramids.

Course. The child died forty-eight hours after operation.

Autopsy. Postmortem examination was made by Dr. L. S. Walsh. Only the part of his findings concerning the lesion will be given. The brain weighed 1300 grams. The basal arachnoid and vasculature were fixed to a mass which displaced cerebral tissue superiorly and indented the floor of the third ventricle and optic chiasm. Gross coronal sections of the forebrain revealed nothing unusual. Gross cross sections of the stem showed scattered subarachnoid clots and two foci of intramedullary hemorrhage each 2 mm. in diameter.

The tumor extending from the base of the brain involved both petrous ridges, the dura along the posterior aspect of the left petrous bone, both middle fossae with complete erosion of the floors, the medial halves of both orbital plates, the ethmoid bone, sphenoid bone and nasal concha. The tumor reached the palate anteriorly and the pharynx posteriorly and extended along both carotid canals and jugular foramina to the retropharyngeal regions.

Histology. The cytologic examination of the specimen showed that it consisted of fibroblastic matrix in which enormous numbers of giant cells were found. There were spicules of bone scattered here and there. The diagnosis was giant cell tumor.

COMMENT

This case presents several interesting features. The rarity of occurrence of giant cell tumors has already received comment. Most giant cell tumors of the skull are in the mandible. However, one case in the sphenoid bone[9] and

two in the frontal bone[2,7] have been reported in addition to the two cases involving the sphenoid bones briefly mentioned by Geschickter and Copeland,[4] which have already been referred to in the opening paragraph.

Another interesting aspect of this case is the fact that the sella turcica was completely destroyed by the growth. To the neurosurgeon, destruction of the sella turcica indicates either obstructive hydrocephalus caused by a tumor in the cerebellar fossa or a large adenoma of the pituitary gland. The possibility of primary tumor of bone was not even considered in this case by the roentgenologist or the surgeon.

Additional points of interest are the lack of a history of trauma and the youthfulness of the patient. Although an occasional case of giant cell tumor of bone has been reported in children, it is generally seen in adults.

The genesis of giant cell tumors has long been a subject for speculation. Probably the most plausible theory is the one expounded by Geschickter and Copeland,[4] who believe that these growths arise from resorptive processes in cartilaginous bone. However, this hypothesis fails to explain the occurrence of such a tumor in the frontal bone (membranous bone), as pointed out by Keegan and Baker.[7]

That the "benign" giant cell tumor sometimes proves to be malignant in its behavior is well known.[1,3,5,6,8] However, even after the tendency of this tumor to destroy the base of the skull became known, there was nothing about its microscopic appearance (Drs. Stewart, Bennett and Schenken) to indicate that it differed from the giant cell tumors that have a truly benign course.

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THE TECHNIQUE OF TANTALUM PLATING OF SKULL DEFECTS

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THE REPAIR of skull defects caused by war wounds or incidental to casual illness among service personnel has become a major responsibility of the military neurosurgeon. A scholarly review of the problem of skull defect repair was presented in 1939 by Grant and Norcross.[4] Since that time, emphasis has been directed toward the use of inert metals or plastics in this procedure and the reports of Geib,[3] Peyton and Hall,[6] Beck,[1] Pudenz,[7] Fulcher[2] and Gurdjian[5] have described the relative clinical merits of vitallium, tantalum and plexiglass (methyl methacrylate).

The strength, malleability and inertness of tantalum in tissue have recommended its use in skull defect repair. Following the experimental demonstration of these qualities by Pudenz, the first tantalum plating of a skull defect in the Walter Reed General Hospital was done by Lt. Col. R. Glen Spurling on 28 September 1942.* This report is concerned with the operative techniques that have evolved during the repair of 42 various skull defects. A later report will include case records in detail.

In the first six cases of this series, small, relatively simple plates were inserted in the skull defects without further fixation. They were preformed by methods to be described and altered to fit at the operating table or formed at the operating table from sheets of .015-inch tantalum plate. After the defect had been exposed, its edges were smoothed and a ledge, several millimeters wide and somewhat deeper than the thickness of the plate, was chiselled out of the outer table of the skull. The fitted tantalum plate was laid upon this ledge without further support.

In the sixth case of this series, following the resection of a cholesteatoma of the occipital bone overlying the torcular Herophili, a tantalum plate was inserted at the primary operation with this simple technique. Fourteen days following operation, while the patient was ambulatory, roentgenography of the skull showed that the plate had slipped from its original position.

In six other cases of this group,† fixation of the plate was secured by wiring the plate through drill holes in the plate and skull with #30 tantalum wire. This proved to be a very adequate method of adjusting less complicated plates to relatively even contours such as those represented by the parietal bone. In such instances, the plate was hammered out at the operating table

* The authors wish to acknowledge and emphasize the pioneering efforts made by Lt. Col. Spurling, former Chief of the Neurosurgical Section, in the development of the techniques described in this paper.

† These six cases were operated upon at the Ashford General Hospital, West Virginia.

and if greater convexity than might be secured by hammering was desired, it was gained by resecting a small, narrow triangle from the plate (Fig. 1).

Such methods for the formation and fixation of the tantalum plate are not easily applicable to the restoration of more complicated contours such as may be present in skull defects involving the frontal bones, including the supraorbital ridges. In the remaining 30 cases of this series, the following techniques for forming and fixing the plates were devised and have been found adequate.

THE TECHNIQUE OF PRIMARY REPAIR

a) *Preparation of the Plate.* The margin of the skull defect is outlined on the scalp with an indelible pencil after removal of the long hair. The scalp and hair are lubricated with vaseline. Dental compound is softened in warm water and molded into the defect and upon the surrounding scalp contours until hard. The outline and depth of the skull defect will be noted as an elevated mass on this primary impression. A model is then poured with dental stone or ordinary plaster. The marking of the indelible pencil will persist on this cast. The depressed area within the cast is filled with wax and contoured to fit the adjacent skull outlines. It is well to overemphasize the convexity of the wax fill to compensate for thin, scarred scalp tissue and for subsequent inlay of the plate. A mold is made with any of the molding sands and a die poured with zinc.* The die is painted with a solution of talc and alcohol. A soft clay, such as moldine, is adapted about the circumference of the die to act as a matrix for the counter die of poured lead. The required size of .015-inch tantalum plate is roughly fashioned with at least a one-centimeter greater diameter than assumed necessary since the defect may be enlarged at operation. The plate is swedged between die and counter die with a hand or hydraulic press. After the initial press, the edges of the plate are smoothed with carborundum and it is polished with an abrasive disc. A single hole, 2 mm. in diameter, is bored in the proposed dependent portion of the plate for drainage purposes and the plate is reswedged. The materials and apparatus required for the formation of such a plate are available in any dental laboratory. Before operation, the plate is cleansed in laboratory cleansing fluid, washed in running water and sterilized in an autoclave.

b) *Operative Fixation of the Plate.* With appropriate consideration of vascular supply and scarring of the scalp, the area of the skull defect is exposed, frequently by means of the standard craniotomy incision. The pericranium is incised one centimeter about the border of the defect and this portion is removed. Indicated bone resection, cerebral scar resection, dural repair, removal of excess tissue or other measures are carried out. With the "lineator" (Fig. 2), the border of the proposed ledge in the outer table is cut circumferentially one-half centimeter from the skull defect. The ledge is formed to a depth slightly exceeding the thickness of the tantalum plate with a Stout #3 dental chisel (Fig. 2). The preformed tantalum plate is adapted to fit the diameter of the ledge by cutting with heavy scissors. With the plate held in place by digital pressure, seats for the tantalum points, much like glazier points, are made with the "perforator" (Fig. 2). The points, usually four to six in number and made of .020-inch tantalum, are tapped into place with the "wedge director" (Fig. 2), completing fixation of the plate.

Since many of the skull wounds have been infected subsequent to the acute injury, sulfanilimide powder is dusted beneath and above the plate and sulfadiazine is given orally for ten days following repair. The craniotomy wound is closed with the customary two layers of interrupted fine silk or nylon sutures without drainage. The repair is carried out in uncomplicated cases under local anesthesia and patients are allowed up within 24 hours.

c) *Illustrative Cases.*

* Studies are now being carried out for these purposes with hydromite, generously provided by the U. S. Gypsum Company.

Case 1. *Primary repair of uncomplicated skull defect with preformed tantalum plate.*

E.D., aet. 31, sustained an extensive, compound depressed fracture of the right frontal and parietal bones with dural and cerebral laceration on 19 July 1943, when a 155-mm. howitzer exploded in action. Primary and secondary debridements were followed by infection

FIG. 1

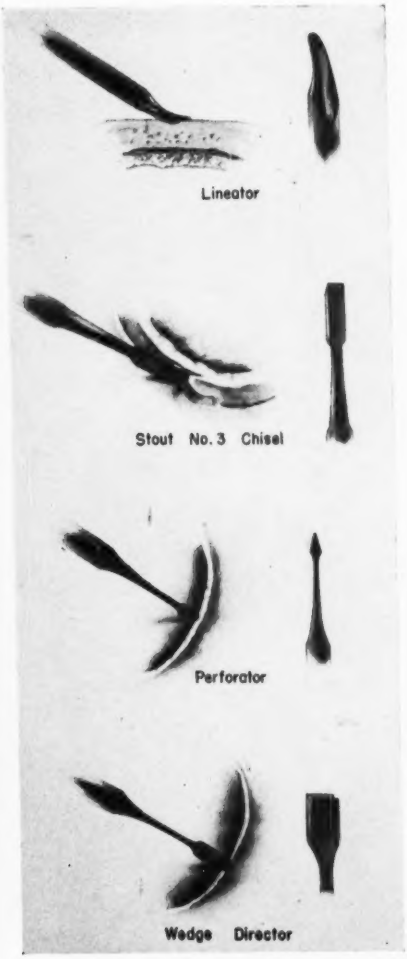

FIG. 2

and the development of a cerebral fungus. On 3 April 1944, a preformed tantalum plate was inserted. Pre- and post-operative roentgenograms show the extent of the bony defect, the plate and the technique of fixation by tantalum points (Fig. 3).

Case 2. *Secondary repair of deforming frontal defect by preformed tantalum plate.*

W.H., aet. 22, developed an acute frontal sinusitis followed by osteomyelitis of the left frontal bone for which an extensive sequestrectomy and bilateral exenteration of the frontal

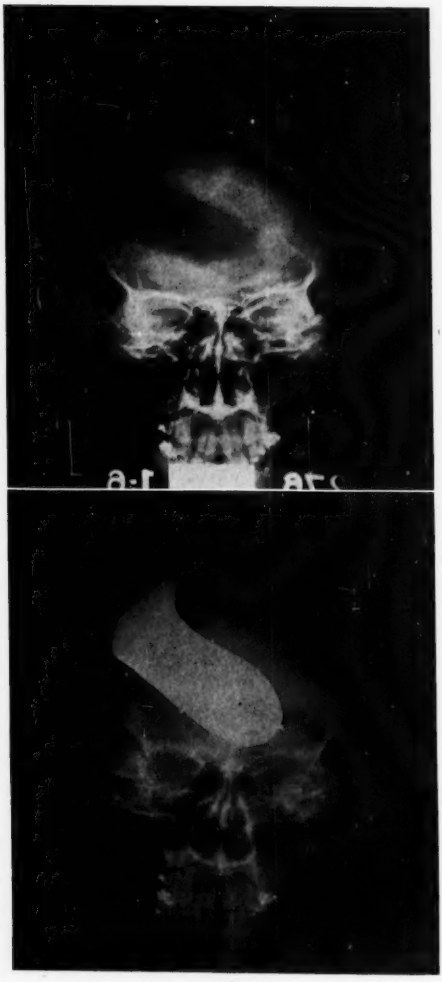

FIG. 3

FIG. 4

sinuses were performed. Four months after the initial procedure, on 28 January 1944, a complicated, preformed tantalum plate was inserted. The extent, contour, and fixation of the plate may be seen in the pre- and post-operative roentgenograms (Fig. 4).

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THE TECHNIQUE OF SECONDARY REPAIR

a) The debridement of bone in acute injuries of the skull, or the removal of a skull tumor or sacrifice of a bone plate following craniotomy may suggest the necessity for a secondary repair of the resultant skull defect. This repair may be facilitated by preliminary preparation of the operative field. After the indicated procedure is completed, the edge of the resulting skull defect is ledged as described previously. An impression of the ledge and the extent of the defect is made with autoclaved dental compound and the tantalum plate is prepared in the usual manner. Prior to closure of the primary wound, a sheet of tantalum foil is placed over the defect, extending well beyond the borders of the circumferential ledge. Experience has indicated that this is an important step in the technique since at the secondary operation for repair, the skull defect and adjacent bone will be found to be uninvolved in scar tissue and not adherent to the overlying scalp. Fixation of the tantalum plate may proceed without further dissection.

b) *Illustrative Case.*

Case 3. *Primary debridement of extensive injury to frontal bones with secondary repair of skull defect.*

E.W.D., aet. 20, was injured on 27 July 1943, when fragments from a dynamite blast struck the right frontal region of the head. On 11 August the comminuted fragments of the medial halves of both supraorbital ridges, the anterior and posterior plates of both frontal sinuses and the adjacent frontal bone were removed. After preparation of a ledge around the defect, an impression was made with sterile dental compound. Tantalum foil was placed over the defect including its edges for a width of one centimeter. On 14 September the primary coronal suture line was reopened and the scalp flap retracted rostrally. In the area where the foil had been placed, there were two glistening, white opposing surfaces with complete prevention of adhesions between the scalp, and the dura and bone. The tantalum plate fitted perfectly and was fixed in position without further alteration.

SUMMARY

The rehabilitation for further duty of Army personnel with skull defects is an ever increasing responsibility of the Army neurosurgeon. Simply contoured tantalum plates may be formed by hammering and fixed in place with tantalum wire. For the formation and fixation of more complicated plates, preformed molding and inlay fixation with tantalum points are indicated and have provided an adequate restoration of skull contour. The various techniques are described and illustrated.

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FUNCTIONAL AND STRUCTURAL CHANGES IN THE MONKEY'S BRAIN DURING AND AFTER CONCUSSION*

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THE PRESENT study was undertaken to check in a primate the functional alterations of simple concussion found in the cat[2] and the histologic alterations demonstrated in the guinea pig.[7] Little previous use has been made of monkeys to study functional aspects of concussion and it would seem that the present histologic results are the first obtained after simple concussion. It is unlikely that autopsy material will ever be available after simple concussion in man but the findings probably would not differ significantly from those in the monkey.

Denny-Brown and Russell[1] employed monkeys, but most of their experiments were performed on cats. So far as their observations went, concussion and subconcussion were the same in the two species. Their protocols of four monkeys show that subconcussive respiratory and blood pressure alterations (with or without section of vagus nerves) were irregular. The concussive phenomena that they observed (with vagus nerves cut) were transitory loss of the corneal reflex, cessation of respiration and steep rise of blood pressure with a gradual decline within about 5 minutes. Concussion was characterized as a condition in which brain-stem centers are inert to reflex activation although they themselves may be in a state of stimulation. Denny-Brown and Russell had the opportunity to observe an intact unanesthetized monkey which was rendered unconscious in the course of an experiment with a model bomb shelter. Percussion injury sufficient to stun the animal abolished the corneal reflex although a lesser injury did not.

Experimentation on cats formed the chief basis for the conclusions of Walker, Kollros and Case,[6] but some monkeys were used and presumably with similar results. They believe that the physiologic basis of concussion consists of depolarization of many nerve cell bodies within the central nervous system caused by the shaking up or vibration of the brain as a result of trauma, and that widespread central and peripheral excitation ensues as axons are fired by this electrical breakdown of the cell membranes. The authors enumerated tetanic phenomena, respiratory, blood pressure, heart rate and spinal reflex alterations and electrical disturbances as evidence for the validity of their theory.

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Shelden, Pudenz and Restarski[4] have studied and demonstrated, by high-speed motion picture photography, brain movements during subconcussive and concussive blows to various parts of the monkey's head. They observed the brain through very large apertures covered by a lucite calvarium.[5] Publication of their most interesting studies on concussion is awaited.

Jakob[3] attempted to investigate histologic changes following concussion in three monkeys. Rabbits formed the bulk of his material. Concussions of doubtful nature were produced in the monkeys by multiple blows. Infection and malnutrition in the animals restrained the author from reporting any observations except some Marchi degeneration.

METHODS AND MATERIAL

Physiologic studies were conducted in acute experiments on 7 rhesus monkeys lightly anesthetized with chloralosane. Only mild concussion could occasionally be produced by means of the pendulum or the hydraulic apparatus previously used on cats. Force applied by either method sufficient to kill a cat would not affect a monkey. Rather than add weight to the pendulum and incur the risk of fracturing the skull, the piston of the hydraulic apparatus was increased in diameter and the falling weight was made heavier. In this way, a force of sufficient magnitude to produce concussion in a monkey could be transmitted to its brain. During the concussion experiment, the state of respiration, corneal reflex, spontaneous motor activity and threshold of stimulus required to elicit appropriate responses of the motor cortex, hypothalamus or facial nucleus were followed and recorded. Adequate recovery intervals were allowed between blows in the same animal. Placement and fixation of electrodes in the brain, stimulation and other details were like those described in concussion experiments in the cat.[2]

Three monkeys that had suffered concussion and one control supplied material for the histologic study. One monkey, No. 6, was from the functional alteration series. It was perfused with 10 per cent formalin (after washing out blood with 1 per cent NaCl solution) at the termination of the experiment. A second, No. 9, was given a light concussion with the hydraulic apparatus and sacrificed 6 days later. In the third, No. 11, severe concussion was produced by striking with a hammer a Wood's metal life-cast attached to the intact head; this specimen was sacrificed after 8 days. Monkeys 9, 11, and the control, No. 10, were given anesthetic doses of nembutal and perfused with 10 per cent formalin (after washing out the blood with 1 per cent NaCl solution).

The brains and spinal cords were carefully removed and the brain stems cut away from the forward parts at the level of the superior colliculus. Each brain stem was placed in 10 per cent formalin for 36 hours; the cerebrum, divided in the midsagittal plane, was placed in formalin for 5 to 7 days. The several pieces of the brain were then embedded in low viscosity nitrocellulose and sectioned at 20μ and 40μ. The stem was cut serially in the transverse plane. Groups of frontal sections were taken at five levels through the hemispheres. The first three segments of the spinal cord were sectioned serially in the frontal plane and horizontal serial sections of the upper part of C4 were prepared. Staining was by the buffered thionin technique (pH 4.3 and 4.9), as in previous studies of concussion changes in the guinea pig.[7]

PHYSIOLOGIC RESULTS

Monkey 1. One bipolar electrode was placed in the face area of the motor cortex (response: contraction of labial musculature) and another in the facial nucleus (response: contraction of labial musculature and eyelid closure). The pendulum apparatus was used. The first three blows were struck on the temporo-parietal region of the skull, corresponding to the area struck

in the experiments with cats. The fourth blow was struck on the external occipital protuberance.

The first blow was strong enough to have produced moderate to severe concussion in the cat. No effect was obtained. The second blow would have produced severe and probably fatal concussion in the cat. A very light concussion was obtained. The corneal reflex was abolished for 25 seconds, respiration paused for 5 seconds, the pupils were dilated and the eyelids opened for 25 seconds. No changes in thresholds were effected. A linear fracture of the skull occurred. The third blow was of the same magnitude as the second. A light to moderate concussion was produced. The corneal reflex was out for 30 seconds; respiration was not interrupted. The threshold of the motor cortex rose from a control value of 2.5 volts to a concussional value of 5.0 volts, with recovery in 15 minutes. The facial nucleus threshold for the labial musculature rose from a control value of 0.9 volt to a concussional value of 1.0 volt. That for eyelid closure rose from 1.4 volts to 1.6 volts. Facial nucleus thresholds recovered in 5 minutes. A circular depressed fracture of the skull occurred. The fourth blow was of the same magnitude as the two preceding. A very light concussion was produced. The corneal reflex was out for 5 seconds and respiration was interrupted for 5 seconds. No change took place in the thresholds. A linear fracture resulted.

Monkey 2. No concussion was produced. The animal was used for another purpose.

Monkey 3. A bipolar electrode was placed in the facial nucleus (response: contraction of the inferior facial musculature). The hydraulic apparatus which had been developed previously for cat experiments was used for this monkey. The cannula of the apparatus was in the parietal bone in a position similar to that used in the cat experiments.

Six blows were delivered. They ranged in intensity from one that would have administered light concussion in the cat to the most severe possible with the apparatus. The last three blows each would have killed a cat. No concussion resulted in the monkey. The more severe blows resulted in short interruption of respiration, blinking of the eyelids, quivering of the trunk and a slight startle.

Monkey 4. A bipolar electrode was placed in the facial nucleus (response: contraction of the facial musculature). The hydraulic apparatus was used. The cannula was placed in the parietal bone.

Eleven blows were delivered. The first seven ranged in intensity from one that would have produced a light concussion in the cat to one almost as severe as was possible to obtain with the apparatus. No concussion occurred in any of these seven blows. The heavier blows caused a startle response and eyelid opening. The heaviest caused, in addition, a respiratory pause for 5 seconds. The four remaining blows each would have produced death in cats. One of them had no effect on the monkey, one caused very light concussion and two produced moderate concussion. The threshold was not affected.

Monkey 5. A bipolar electrode was placed in the hypothalamus (response: pupillary dilatation). The same hydraulic apparatus was used.

The first four blows ranged in intensity from one that would have produced a moderate concussion in a cat to one that would have proved fatal. No concussion occurred in the monkey. The fifth blow did produce a moderate concussion. The corneal reflex was abolished for 15 seconds and respiration ceased for 15 seconds. The threshold rose from a control value of 1.4 volts to a concussional value of 1.8 volts. Recovery occurred in 2 minutes. The sixth and seventh blows produced no concussion. The eighth blow produced a moderate concussion. The corneal reflex was out for 65 seconds and respiration ceased for 10 seconds. No alteration in threshold was observed. Any one of the last four blows would have proved fatal in the case of the cat.

At this stage an hydraulic apparatus with a piston greater in diameter was devised. Subsequently, as noted in the following protocols, more weight was added to the disc that dropped onto the piston. Thus, we obtained an apparatus capable of delivering such force that even severe concussions could be produced without calling upon the maximum output of the apparatus. This meant hitherto unavailable controllability of concussions.

Monkey 6. A bipolar electrode was placed in the facial nucleus (response: eyelid closure). The remodeled hydraulic apparatus was used and the cannula was in the parietal bone.

The first five blows produced no concussion and only a slight startle response. The force applied was increased successively by closing by degrees the needle escape valve in the hydraulic system. The sixth blow was more severe than the preceding ones and produced a moderate concussion. The corneal reflex was abolished for 20 seconds but respiration was not affected. The pupils dilated and the eyelids opened. The threshold to stimulation rose from a control value of 1.8 volts to a concussional value of 3.0 volts; there was no recovery in 10 minutes. Blow seven was more severe than number six and it produced a moderate concussion. The corneal reflex was out for 25 seconds, respiration ceased for 25 seconds, the pupils dilated and the eyelids opened. The threshold to stimulation rose from a control value of 3.0 volts to a concussional value of 3.5 volts and there was recovery in approximately 10 minutes.

At this point in the experiment, additional weight was added to the disc that dropped upon the piston. The eighth blow was more severe than number seven. A moderate to severe concussion was induced. The corneal reflex was abolished for 75 seconds and respiration ceased for 25 seconds. The pupils dilated. The threshold rose from a control value of 3.0 volts to a concussional value of 3.5 volts. There was no recovery in 22 minutes. The ninth blow was one of the same magnitude as the eighth, resulting in a moderate concussion. The corneal reflex was out for 25 seconds and respiration ceased for 60 seconds. The pupils dilated. There was no increase in the threshold to stimulation. The tenth blow was approximately of the same mag-

nitude as number seven. It gave a moderate concussion. The corneal reflex was out for 20 seconds, as was respiration. There was no increase in threshold to stimulation. The eleventh blow was the most severe of all, more weight having been added to the disc. A moderate concussion was produced. The corneal reflex was out for 25 seconds and respiration ceased for 35 seconds. No threshold changes occurred.

In all of these concussions, a startle or a struggle was observed upon delivery of the blow. Stimulation in the facial nucleus, besides eliciting the primary response of lid closure, also evoked a secondary struggle response. The threshold for this latter response showed greater elevation and slower recovery than that for the eyelid closure response.

Monkey 7. A bipolar electrode was placed in the facial nucleus (primary response: contraction of the facial musculature; secondary response: contraction of the abdominal musculature). The same hydraulic apparatus that was used in the preceding experiment was employed, but the weight of the disc that was dropped upon the piston was substantially increased.

The first blow produced a moderate concussion. The corneal reflex was abolished, although the time during which it was out was undetermined. Respiration ceased for 10 seconds. The threshold for the facial musculature response rose from a control value of 0.9 volt to a concussional value of 1.0 volt. The threshold for the abdominal musculature response rose from a control value of 1.0 volt to a concussional value of 2.0 volts. We were unable to determine the recovery time because a secondary cessation of respiration intervened. Artificial respiration was successfully applied for a short time, following which the experiment was terminated.

Monkey 8. A bipolar electrode was placed in the forelimb area of the motor cortex (response: forelimb movement). The same hydraulic system was used as in the previous experiment, with the cannula in the left parietal bone.

The first blow produced a light concussion. The corneal reflex was out for 15 seconds and respiration ceased for 10 seconds. The threshold rose from a control value of 5.0 volts to a concussional value of 6.0 volts. Recovery occurred in 13 minutes. The second blow was stronger than the first and produced a light to moderate concussion. A startle was noted at the instant of the blow. The corneal reflex was abolished for 20 seconds and respiration ceased for 7 seconds. The threshold to stimulation rose from a control value of 5.0 volts to a concussional value of 7.0 volts. Recovery took place in 31 minutes. A third blow was stronger than the second and produced a severe concussion. A startle occurred and the pupils dilated. The corneal reflex was abolished for a prolonged period of time and respiration ceased. The threshold to stimulation rose from a control value of 5.0 volts to a concussional value of 20 volts. Recovery of the corneal reflex and the threshold to stimulation occurred but was delayed. Artificial respiration was begun one minute after the blow and was successful. Ten seconds after the blow, the animal

slowly became tense and quivered. This general spasm gradually subsided over a 30-second interval.

HISTOLOGIC RESULTS

The most marked histologic changes were observed in the brain of Monkey 11, which was the animal struck upon a Wood's metal life-cast affixed to the calvarium with scalp intact. Four blows were struck with the following effects: blow 1, corneal reflex was not affected, respiration paused for 5 seconds; blow 2, corneal reflex was abolished 60 seconds, respiration ceased for 15 seconds; blow 3, corneal reflex and respiration both were abolished for 30 seconds; blow 4, corneal reflex was abolished for 5 seconds, respiration ceased for 20 seconds. Sufficient interval for complete recovery was allowed between blows. The animal was sacrificed 8 days later.

Throughout the brain stem much evidence of cytologic alteration was observed, though not in all of the cell groups. None of the primary motor nuclei exhibited damage. The changes appeared to be very largely confined to interneuron systems. Both large and small nerve cells were affected, the former most strikingly. Large neurons of the red nucleus, the pontile reticular formation, vestibular nuclei, superior olivary nuclei and the lateral reticular nuclei showed chromatolysis. Some of these cells were so completely destroyed that their remnants could be observed only by very careful study with a high-power lens. Many contained no Nissl bodies. In the upper cervical segments of the spinal cord, damage was confined to small and medium-sized nerve cells, especially those of the posterior grey columns.

It is impossible to estimate accurately the proportion of neurons affected by concussion. Ten per cent of those in the reticular formation is perhaps a reasonable guess for this one specimen. The amount of damage was less in this monkey than in some of the more severe concussions in guinea pigs.

In Monkey 9, light concussion was produced with the hydraulic apparatus. Aseptic technique was employed. The first blow did not affect the corneal reflex and caused a respiratory pause of only 8 seconds; upon the second blow, the corneal reflex was unelicitable for 12 seconds and respiration ceased for 10 seconds.

Histologic changes were observed, and their distribution in the brain stem was similar to that of No. 11. Structural alterations were slight and few cells were in a state of marked chromatolysis. There seemed to be nearly as many of the smaller interneurons of the brain stem affected as in the monkey that was struck with a hammer. Lower motor neurons of the brain stem were not affected. However, in the upper cervical spinal cord a few anterior horn cells showed mild central chromatolysis unlike that usually observed after concussion. These cells occurred in one thin linear column in the ventrolateral portion of the grey matter of one side and were not found elsewhere; most were found in a single 40μ section.

Monkey 6 was one that received many blows with the hydraulic system in the course of an experiment on functional alterations. This animal was perfused at the conclusion of the experiment. It provided material for the study of changes immediately after concussion. Some large neurons, especially those of Deiter's nucleus and the red nucleus, appeared to have suffered change. Comparison with the control specimen, No. 10, gave indication that the Nissl bodies had been fragmented and their pattern disorganized. The condition was not nearly as well defined, however, as in the guinea pigs in which perfusion with 10 per cent formalin was carried out immediately upon striking a blow.

Parts of the brain rostral to the mesencephalon showed less marked alterations after concussion. Eight days after concussion, in Monkey 11, changes were clearly observed only in the large motor cells of the cerebral cortex. These large pyramidal cells appeared shrunken, hyperchromatic and showed disturbances of the Nissl-body pattern. None of them was chromatolyzed. The changes are illustrated in Fig. 3.

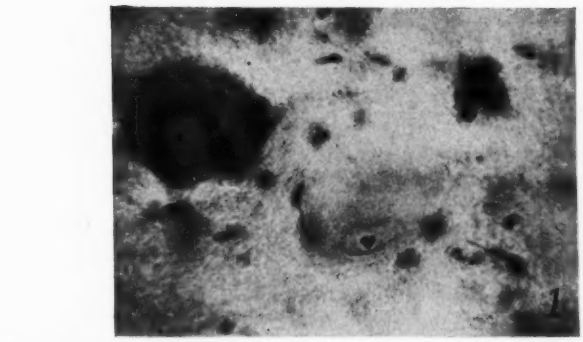
The monkey that received two light blows with the hydraulic apparatus and was sacrificed six days later showed similar changes in the pyramidal cells of the motor cortex. These differed distinctly from the cells of the same region of the control animal and in the animal that was sacrificed at the conclusion of an acute experiment.

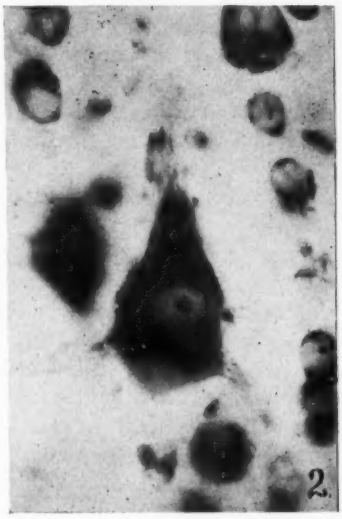
We were unable to observe structural changes in the cortex of the cerebellum. The various portions of the thalamus appeared to be little, if any, involved in structural alterations. The basal ganglia of the cerebrum and the cell groups of the hippocampus seemed to be normal. It is quite possible that more extensive investigation of structural changes in monkeys receiving blows of greater severity would reveal losses and damage which these few experiments failed to do. Nevertheless, it is clear that a differential effect like that in the guinea pig[7] took place with damage of certain neurons, especially in the brain stem, after adequate force was applied to the brain of the monkey.

In none of our sections did we find even slight interstitial hemorrhages. There was no indication of any reaction about walls of blood vessels in the brains of monkeys that had suffered concussion. No glial reactions could be identified. Nerve fiber tracts showed no degenerative phenomena. The swelling of myelin sheaths seen in brains of guinea pigs after severe concussion was not observed in the monkey. In short, cytologic alterations were ascribable to uncomplicated concussion of the brain.

DISCUSSION

The present physiological experiments in rhesus monkeys demonstrate a differential change upon concussion of the brain similar to that reported in the cat.[2] Function of the motor cortex of the cerebrum and of other supranuclear motor regions was more adversely affected than was function of cranial motor nuclei. The latter usually exhibited slight or no elevation in





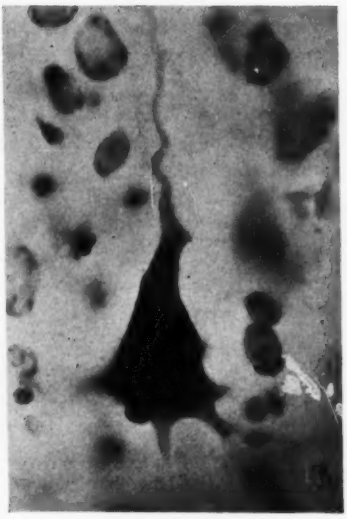


FIG. 1. Two spinal interneurons from the base of the dorsal grey column of the first cervical segment of Monkey 11. The cell on the left is normal; that in the center is severely affected by concussion and has undergone chromotolysis. (×550)

FIG. 2. Large pyramidal cell from the motor cortex of control Monkey 10. Compare with Fig. 3. (×550)

FIG. 3. Large pyramidal cell from the motor cortex of Monkey 11. The cell is shrunken, hyperchromatic, and exhibits "corkscrew" dendrites. (×550) Preparations illustrated in Figs. 2 and 3 were stained at pH 4.3.

threshold of stimulation immediately after a concussive blow had been struck. In five instances in which the corneal reflex was abolished long enough to make trustworthy observations, the threshold of the facial motor nucleus for eyelid closure was unchanged in concussion, although the corneal reflex itself was absent. When one considers the present physiological experiments together with those of Denny-Brown and Russell,[1] there appears to

be no doubt that functional alterations of brain concussion are the same in the rhesus monkey and the cat.

Our experiments suggest that the major feature of concussion of the brain is a transient paralysis of certain interneuron systems. The excitatory phenomena which we have observed in concussion in cats, monkeys and guinea pigs lightly anesthetized with chloralosane have been isolated, occasional and variable. In the monkey, possible evidences of stimulation were elevation of the upper eyelids, dilatation of the pupils, and struggle. In the cat they were dilatation of the pupils, withdrawal of the nictitating membrane, tonic contractions of the orbicularis oculi muscle, tonic contractions of the tongue musculature, and reduced thresholds of cranial motor nuclei and fiber bundles. In the guinea pig, tonic or clonic spasm of limb or trunk musculature was apt to occur at any time in the minutes following the blow. It is to be emphasized that all these manifestations were of isolated and occasional nature. The startle reflex which often could be observed upon impact in monkeys and cats was very slight and qualitatively was the same as, though in magnitude much less than, the startle response which could be elicited prior to concussion by clapping the hands or striking the table in the proximity of the animals.

The correlation between our physiologic results and our histologic observations is evident. Histologic alterations were encountered in certain upstream interneuron systems, including the motor cortex, but were most extensive and severe in the brain stem.

It should be emphasized that in experiments with monkeys, we were dealing with simple concussions, i.e., transient paralytic states setting in immediately upon application of an adequate force to the brain. In human clinical experience, concussion is often combined with traumatic interstitial hemorrhage, contusion or laceration of the brain. The latter three types of injuries should not be given the unmodified designation, concussion. We would caution further that the several post-traumatic conditions should not be referred to loosely as concussion. Indiscriminate use of the term concussion and its equivalents has produced much confusion in the realm of traumatic brain injuries and their sequelae. We hope the present study will help form a basis for limiting its use.

SUMMARY

Concussions of the brain were induced in rhesus monkeys by striking the head with a pendulum apparatus, by dropping a weight on the piston of an hydraulic apparatus connecting with the interior of the cranium by means of a metal cannula, or by striking with a hammer a Wood's metal lifecast applied to the head. In acute physiologic experiments, it was demonstrated that differential functional alterations took place in the monkey as they did in the cat. Function of the motor cortex of the cerebrum and of other supranuclear regions was more adversely affected in concussion than was function of cranial motor nuclei. Corneal reflexes could be abolished

without significantly changing the threshold to stimulation of the motor neurons involved.

Histologic alterations were observed in the brains of monkeys that had been struck concussive blows six or eight days previously. These consisted of differential chromatolytic changes in certain interneuron systems of the brain stem and of other cytologic changes in the pyramidal cells of the motor cortex. Primary motor neurons of the cranial nerve nuclei were not affected. Immediate cytologic changes similar to those described previously in guinea pigs were observed in certain large neurons of the monkey's brain. The structural changes appeared to be ascribable to uncomplicated concussion of the brain.

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POST-TRAUMATIC VERTIGO AND DIZZINESS*

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INTRODUCTION

A COMMON complaint following head injury is a sense of rotation of objects or of the patient himself, that is, a true vertigo, or a less specific sense of movement referred to as "dizziness" and "giddiness." Although giddiness often occurs as a part of the post-traumatic syndrome (of which the other prominent features are headache, emotional lability, and difficulty in mental concentration), it may be present alone.

Statistics on the frequency of occurrence of dizziness following trauma vary somewhat from author to author. Glaser[5] in a series of 325 cases of head injury found dizziness in 60 per cent of the patients following trauma. Linthicum and Rand[8] in their series of 36 cases reported vertigo in some form in approximately 90 per cent of their patients, but used the term to include some degree of equilibratory disturbance ranging from a mere feeling of uncertainty to actual systematized vertigo. Osnato and Giliberti,[10] in an analysis of 100 cases of concussion with or without fracture, grouped dizziness and giddiness under one heading and found it present in 57 of their patients. Schuster[14] reported that 40 per cent of all head injuries produce ear symptoms. Russell[12] analyzed 200 consecutive case records of head injury in which dizziness was noticed in 21 cases. True vertigo was not present in any of the cases examined. The discrepancies between these figures may be partly explained by the differences in material and the sub-categories included under dizziness by the various investigators.

In a discussion of dizziness *per se* following trauma, or as a part of the post-traumatic syndrome, there are many opinions as to what are the important factors in the evaluation of dizziness. In general there are three schools of thought—one group who consider dizziness, as well as the other symptoms of the post-traumatic syndrome, to be of psychogenic origin; another group who report it to be exclusively of physiogenic origin; and others who emphasize the importance of both types of factors.

Grove[6] in a survey of the subject remarked that post-concussional vertigo of vestibular origin is characterized by a systematized dizziness accompanied by nystagmus brought on by movements of the head. He considered other types of equilibratory disturbance to be of psychoneurotic origin. Rowbotham[11] expressed the opinion that the headache and dizziness of the post-

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concussional syndrome have a direct organic basis in contrast to tremor, anxiety, and general nervousness which are due to a neurosis. Schaller[13] includes dizziness under "post-traumatic psychoneurotic state." Symonds,[15] Lewis,[7] and one of us[4] emphasize the importance of both physiogenic and psychogenic factors in the post-traumatic syndrome. They further state that the practice of labelling the syndrome organic in one and functional or neurotic in another is unprofitable and misleading. The purpose of this investigation was to study such factors in relation to post-traumatic dizziness in a group of civilian head injuries admitted to a general hospital.

METHOD

The present report is based on a series of 200 consecutive head injuries admitted to the Boston City Hospital. Selection to some extent was inevitable, for the requirements of the inquiry necessitated that all cases where the essential data on duration of loss of consciousness were complicated by alcoholic stupor or other unrelated complications be excluded. Further, since the main objective of the inquiry was related to disability in persons in regular occupations, uncomplicated by the effect of age or difficulty in follow-up, the study was limited to age groups between 15 and 55 years and excluded chronic alcoholics and chronic unemployed. The material, selected in these respects, was fairly evenly distributed in the age group 15–54, and consisted of 125 males and 75 females of a variety of national stocks (71 predominantly Irish) and occupations (96 skilled or semi-skilled workers).

The patients were studied as soon as they were brought into the hospital, which in most cases was within a few hours after the accident. They were then followed daily during their hospital stay and after discharge in the out-patient clinic at intervals of one to two months for periods of six to fifteen months. On each follow-up visit each patient was seen by a neurologist, psychiatrist, psychometrist, electroencephalographer, and social service worker. Roentgenograms, spinal fluid examinations, electroencephalograms, and other laboratory procedures were done when possible during the hospital stay and whenever necessary in the course of the follow-up. The following factors concerning each patient were especially noted—locations of any scalp or skull injury, signs of brain injury, any bleeding from the ears, deafness, disorders of the drums, and any previous history of vertigo or aural disease. The patient was questioned as to when the vertigo was first experienced, whether there was any definite sense of motion, whether he felt that objects were moving or whether he was, the effects of posture, effort, both physical and mental, duration and frequency of attacks, associated symptoms, what relieved and what aggravated the attacks, and his affective state. The routine tests such as Weber, Rinne, coin test, whispered voice, etc. were carried out in all cases.

RESULTS

Dizziness or vertigo following head injury was always intermittent in the group of patients seen by us. Each attack was of variable duration, usually lasting a few minutes. The severity and frequency of the attacks were likewise quite variable. The outstanding precipitating factor was change in posture, whether sudden or otherwise. This factor was present in 53 (78 per cent) of the 68 patients with dizziness during convalescence. In 9 other patients (13 per cent) emotional stress was reported as a precipitating factor. Relief from an attack was generally sought by lying or sitting down and often by closing the eyes, and these simple proceudres were usually felt by the patient to be of value.

Ninety-nine (50 per cent) of the 200 patients complained of dizziness at

some time after injury. Sixty-eight patients (34 per cent) complained of dizziness after hospital discharge, while 31 (16 per cent) were dizzy during their hospital stay, but not thereafter. Eleven patients (6 per cent) complained of true vertigo at some time after injury. The total of patients who complained of either dizziness or vertigo at some time after injury was 102 (51 per cent). It might be of interest to compare these figures with those for the incidence of headache in the same group of patients as previously reported.[2]

Of the total of 68 patients complaining of dizziness in convalescence 52 complained also of headache and 46 of mental symptoms (anxiety, neuroses, depression, etc.). Of 81 patients complaining of headache 55 complained of mental symptoms. Seventy patients complained of mental symptoms alone

TABLE 1

	Present at any time after injury		Persisting after hospital discharge	
	No. Cases	Per cent	No. Cases	Per cent
Dizziness (excluding vertigo)	102	51	68	34
Headache	138	69	81	41

in convalescence. The patients complaining of true vertigo will be discussed in a separate section.

POST-TRAUMATIC DIZZINESS

A. *Correlations with Psychiatric Evaluation and Factors Indicative of Psychological Reaction to Injury* (Table 2). The incidence of dizziness lasting longer than two months after injury was significantly high in the following groups of patients: (1) those patients who were considered to have been neurotic or generally nervous prior to the accident; (2) those patients who after discharge from the hospital complained of fears, anxieties, fatigability, irritability, and inability to concentrate; (3) those patients with complicating environmental factors which might conceivably increase their emotional strain. Of these factors occupational difficulties and pending litigation or compensation had the greatest statistical importance, the former more than the latter. Less striking positive differences were observed in those patients who exhibited obvious emotional reaction immediately following injury.

B. *Correlations with Factors Related to Severity of Injury* (Table 3). The incidence of post-traumatic dizziness lasting longer than two months was significantly high in those patients who had a measurable retrograde amnesia, post-traumatic amnesia, and disorientation, and rose with increasing durations of these. However all 5 patients who suffered from disorientation for over 14 days had no dizziness in convalescence. The presence of a measurable interval of initial coma was associated with twice as high a frequency of prolonged dizziness as when coma had not occurred. Conversely, the in-

TABLE 2

Correlation between duration of dizziness and factors related to mental reaction to head injury

	Duration of Dizziness					
	None		Less than 2 months		More than 2 months	
	No. Cases	Per Cent	No. Cases	Per Cent	No. Cases	Per Cent
Pre-Traumatic Psychiatric Evaluation						
Normal	62	70	10	11	17	19
Neurotic or nervous	13	49	2	7	12	44
Psychopathic personality	20	60	5	14	9	26
Immediate Post-Traumatic Emotional Reaction (excluding confusion)						
None, or other reactions such as apathy, restlessness	110	69	18	11	31	20
Predominant emotional reaction	9	56	2	13	5	31
Late Post-Traumatic Mental Reaction						
None	108	83	14	11	8	6
Fears, anxieties, fatigue, inability to concentrate, nervousness, irritability	17	29	7	12	35	59
Complicating Environmental Factors						
None	60	83	7	10	5	7
Pending litigation	16	47	4	12	14	41
Occupational difficulties	3	27	2	18	6	55

TABLE 3

Correlation between duration of dizziness and factors related to severity of injury

	Duration of Dizziness					
	None		Less than 2 months		More than 2 months	
	No. Cases	Per Cent	No. Cases	Per Cent	No. Cases	Per Cent
Duration of Disorientation						
None	12	67	4	22	2	11
Less than 1 hour	67	72	6	6	20	22
1 to 12 hours	39	63	10	16	13	21
More than 12 hours	14	52	2	7	11	41
Retrograde Amnesia						
None	15	66	4	17	4	17
Momentary	86	70	14	11	24	19
Minutes or more	31	58	4	8	18	34
Post-Traumatic Amnesia						
None	12	71	4	24	1	5
Less than 1 hour	73	72	6	6	22	22
1 to 12 hours	32	59	10	19	12	22
More than 12 hours	14	52	2	7	11	41

cidence of post-traumatic dizziness lasting two months was significantly low in the following groups of patients: (1) those who had no disturbance of consciousness or who were only dazed as a result of the injury; (2) those who suffered no post-traumatic amnesia or disorientation following the injury.

TABLE 4

Correlation between duration of dizziness and miscellaneous factors

	Duration of Dizziness					
	None		Less than 2 months		More than 2 months	
	No. Cases	Per Cent	No. Cases	Per Cent	No. Cases	Per Cent
Sex						
Male	86	69	12	10	27	21
Female	46	61	10	14	19	25
Age						
15–19 years	29	80	2	6	5	14
20–29 years	31	65	8	16	8	19
30–39 years	28	67	7	16	5	17
40–49 years	29	57	5	10	13	33
50–55 years	14	61	0	0	7	39
Duration of Headache						
None	103	78	9	7	20	15
Less than 2 months	9	41	7	32	6	27
2 to 6 months	5	33	1	7	9	60
Over 6 months	2	6	1	4	28	90
Relation of Headache to Other Factors						
None	103	86	9	8	7	6
Posture	11	44	5	20	9	36
Effort or fatigue	5	23	4	18	13	59
Emotional upset	3	27	1	9	7	64
Absence from Full Employment After Injury						
Less than 7 days	38	91	3	7	1	2
Within 1 month	49	69	7	10	15	21
Within 2 months	13	57	3	13	7	30
2 to 6 months	9	45	2	10	9	45
Over 6 months	4	29	0	0	10	71

C. *Miscellaneous Correlations* (Table 4). There was good correlation between the duration of dizziness and the duration of headache, showing the relationship of these two symptoms in the post-traumatic syndrome. There was also striking but not complete correlation between the duration of dizziness and duration of absence from full occupation following injury. The low incidence of prolonged dizziness in the group of patients who were able to return to work within 7 days after injury was in marked contrast to the high incidence among those who were out of work for longer periods. The longer the dizziness persisted, the longer the period before the patient was able to

return to work. A greater proportion of the patients who complained of headaches precipitated by emotional upsets, effort, or fatigue had dizziness of longer duration than those patients with headaches not precipitated by these factors. The sex of the patient played but a slight part in the incidence of prolonged dizziness. The effect of age was notable in a moderate increase in incidence and duration of dizziness over the age of 40 years.

There was no correlation between the incidence of dizziness and the following factors—abnormalities in tendon reflexes or plantar responses immediately after injury, pressure of cerebrospinal fluid on first or subsequent lumbar puncture or the presence or absence of blood in the fluid, the presence of signs of skull fracture, localizing neurological signs, intellectual status of the patient, duration of physical signs, educational status, or presence or degree of E.E.G. abnormality in the first week after injury.

VERTIGO

Definite vertigo was the complaint of 11 patients. The symptom appeared in two different ways. In four patients vertigo appeared for the first time in spontaneous attacks at intervals of $1\frac{1}{2}$, 2, 3 and 10 months after injury. Two of these patients did not complain of either vertigo, dizziness, or deafness while in the hospital and had no evidence of damage to the middle ear. The other two patients complained of dizziness while in the hospital without other evidence of damage to the labyrinth. In only one of the patients did tinnitus and deafness develop, and these at intervals of two and four months after the injury respectively. In these four patients the relationship between injury and subsequent vertigo therefore remains doubtful for none had evidence of damage to the ear immediately after the injury.

In the remaining seven patients vertigo occurred in the period immediately following the injury. One had initial bleeding from the ears, bilateral deafness, and sixth nerve weakness, with postural vertigo lasting six weeks. Two had immediate diplopia and vomiting after injury but no evidence of damage to the ear. Postural vertigo lasted for one year in one of these two and became converted to postural dizziness of similar duration in the other. One further patient had a mild injury, falling on the back of the head, but had unequal pupils and immediate postural vertigo with occasional spontaneous attacks lasting for seven months, and one had a sudden violent backward displacement of the head with vomiting and postural vertigo for over 6 months. The two remaining patients suffered from transient vertigo lasting two and four days after relatively trivial injuries without other signs.

The absence of evidence of damage to hearing or of bleeding into the middle ear or auditory meatus in all but one of these cases leaves considerable doubt as to the mechanism of the vertigo. In four patients there was evidence that could be interpreted as damage to the brain stem (diplopia, unequal pupils, nystagmus, vomiting, extensor plantar response) and such damage could not be excluded in the one patient with bleeding from the ears. We are inclined to favor this explanation in the absence of more convincing evidence of damage to the labyrinth. We can put forth no evidence to sup-

port a relationship between a head injury and the development of Ménière's syndrome after two months in one patient and record this as a possible coincidence in a man 53 years of age.

BLEEDING FROM THE EXTERNAL AUDITORY MEATUS AND LABYRINTHINE CONCUSSION

Direct damage to the bony labyrinth by a cranial fracture is an obvious possible cause of prolonged vestibular disorder. It is remarkable, however, that where there was clear evidence of the possibility of such damage, dizziness and vertigo were remarkably infrequent. There were 16 cases in the present series where bleeding from one or both ears was found after injury. Only 5 of these had dizziness in convalescence, a proportion smaller than in the remaining cases. In most of these any associated deafness cleared in two to five days. In two patients a severe deafness remained, and in one of these a vertigo related to posture lasted for six weeks.

There is, therefore, little support for the thesis that post-traumatic dizziness is derived from labyrinthine trauma. It is possible, however, that the common mechanism of traumatic hemorrhage from the meatus does not necessitate equivalent damage to the labyrinth, and the infrequency of persistent deafness suggests that this is so. Concussion of the labyrinth is an entity more difficult to exclude. It is considered likely, however, that labyrinthine concussion should exhibit the characteristics of concussion of other nervous structures, namely an initially maximal disturbance of function followed by progressive lessening of disorder. Immediate, severe, true vertigo was encountered in only six cases, in five of which vertigo or dizziness reappeared in convalescence. In two of these, the absence of deafness and presence of signs of damage to the brain stem appeared to exclude labyrinthine damage. There were, therefore, only three patients in whom labyrinthine concussion appeared to be a possible explanation for subsequent vertigo or dizziness. Only one of these had deafness, and in this case and in one other the vertigo ceased within eight weeks. In the remaining patients vertiginous attacks, mostly spontaneous in nature and characteristic of other types of Ménière's syndrome, occurred for six months after the injury.

DISCUSSION

The high degree of correlation between the incidence of dizziness lasting for longer than two months and the incidence of similarly persistent headaches and nervous symptoms is, of course, merely a statistical reflection of the well known association of these symptoms in the post-traumatic syndrome. That this syndrome is frequently associated with prolonged occupational disability is also well known and this fact, too, is borne out by our results. The chief subject of investigation in the present paper has been dizziness, and our attention will naturally be focussed on that symptom in the discussion.

The most striking relationships that we have demonstrated are those between the incidence of prolonged dizziness and various factors of psychiatric

significance: pre-traumatic nervous or neurotic symptoms, complicating environmental factors during convalescence (particularly occupational difficulties and compensation), and immediate emotional reaction to the injury. These relationships point to the importance of psychological factors in the production and/or continuation of post-traumatic dizziness. We wish, however, to warn against any unwarranted attempt to oversimplify the problem. A glance at the accompanying tables will show, for example, that even of the patients with pending litigation or occupational difficulties only about one-half complained of dizziness for two months or longer. The other 50 per cent were either entirely free from this symptom, or complained of it for only a short time. Similarly, just under half of all patients with pre-traumatic nervous symptoms were entirely free from dizziness during convalescence. In a word, the relationships under discussion are significant only for the group, and not necessarily for each individual case.

The correlations in Table 2 indicate that not only emotional factors, but also the physical trauma of the injury itself is significant in the production and continuation of post-traumatic dizziness. Patients with trivial head injuries, as evidenced by absence of coma, disorientation, and post-traumatic amnesia, had a strikingly low incidence of prolonged dizziness, while those with disorientation or amnesia lasting for longer than 12 hours had an equally high incidence of prolonged dizziness. We conclude from these facts that the severity of the injury to the cranial contents is an important factor in the causation of post-traumatic dizziness, and that in the majority of cases of long continued post-traumatic dizziness both physical and psychological factors are important and operative. Attention is called to the similarity between these conclusions and those concerning the causative factors of headache in the post-traumatic syndrome which were advanced in our recent communication on that subject.[2]

We wish to point out again in this connection that the relationship between the incidence of continued dizziness and severity of injury is a statistical and not an absolute one. Ten per cent of the patients with no coma or disorientation after injury nevertheless had persistent dizziness, while more than 50 per cent of those with disorientation and amnesia lasting for more than 12 hours after injury complained of no dizziness whatever during convalescence.

Since Bennett[1] described lability in the pulse rate and volume in the patient suffering from post-traumatic symptoms, a vasomotor disorder directly resulting from the injury has frequently been held responsible for post-traumatic postural dizziness. McKenzie[9] has recently emphasized the precipitation of dizziness by postural change, and believes that an injured and therefore unstable vasomotor system is at fault. To test this hypothesis 11 patients in our series were given tilt-table tests. In this group the length of time after injury was from 24 hours to over nine months and the type of injury varied from slight to severe. Of these patients, eight were complaining of postural dizziness or vertigo.

The patients were placed on the tilt table in the horizontal position for

10 minutes followed by head-down position (30°) for 10 minutes. They were then tilted head up (70°) for 20 minutes. Changing position from head down to head up was done in 50 seconds or less in all cases except one which took 90 seconds. Throughout the tilt-table experiment symptoms and signs of circulatory changes were noted and recorded and included blood pressure records, pulse records, observation as to color, and temperature of skin, sweating, syncope, testing of auditory and visual perceptive changes and subjective changes such as headache, dizziness, nausea, tinnitus, etc.

The results showed moderate vasomotor changes (flushing of the face, or sweating, or cold extremities) and slight changes in blood pressure and pulse in all cases as the position of the head varied. These reactions were not greater than those commonly found in normal controls. Two patients complained of headache slight in degree and transitory in duration, and one patient complained of nausea, while none complained of dizziness or vertigo. None complained of headache, dizziness or nausea on return to head-up posture.

We are therefore not convinced that vasomotor instability was profoundly changed in this small group of patients. It is possible that more rapid swing from head down to head up would give a definite response in such patients, but the postural reaction then would also affect a number of subjects without head injury.

True vertigo was present in 11 patients in all and in only 9 during convalescence after hospital discharge. Only one was considered to be related to labyrinthine injury, and in five brain stem injury was considered the probable cause. The remaining patients had no demonstrable evidence of localized damage that might be related to their vertigo. However, there was a more significant correlation between severity of injury as shown by duration of post-traumatic amnesia or disorientation in those patients with prolonged dizziness than those complaining of persistent headache.

Another notable finding was the persistence of the symptom. It was still present at the last follow-up visit (6 to 12 months after the injury) in 8 of the 11 patients, though 5 of these 8 had already returned to work despite the persistence of this symptom, and one another was about to return. Of the two remaining patients, one was a professional dancer whose vertigo was specifically disabling because of his occupation, while the other was a butcher whose disability was due partly to an associated injury to his right hand and partly to his attacks of vertigo and persistent diplopia.

An interesting fact about this group of patients was the variation in symptoms during the post-traumatic course. Of the 9 patients whose true vertigo outlasted their hospital stay, 2 complained originally of true vertigo and later of non-specific dizziness, while 2 complained first of dizziness and only later of true vertigo. This latter finding may be in part a reflection of the difficulty that patients have in observing and reporting accurately subjective sensations during an attack, but is probably also an indication of a closer relationship between non-specific dizziness and so-called true vertigo than many authors have hitherto been willing to concede. It is certain at

any rate that in two of our patients convalescence was marked by a transformation of the attacks of true vertigo into attacks of non-specific dizziness and then by a gradual amelioration in the severity of the feeling of dizziness during the attacks.

Spontaneous attacks of vertigo occurred in 4 patients, in each case at an interval after the injury. In one of these the delayed appearance of progressive deafness and tinnitus was characteristic of Ménière's syndrome; in the others this evidence did not appear. It is possible that the associated symptoms may develop later in these, but one has since died of carcinoma, and although the liability to vertiginous attacks continued in the remaining two for periods of 12 and 8 months, the only complication has been a severe neurosis in each patient. It may be remarked, however, that according to Colledge[3] the pathological evidence of damage to the vestibular labyrinth, even in cases where traumatic hemorrhages were found in the cochlea, has not been found by histological investigation. There is, therefore, little evidence of a traumatic mechanism for Ménière's syndrome.

SUMMARY

1. Two hundred consecutive hospitalized cases of head injury between the ages of 15 and 55 years exclusive of chronic alcoholics and vagrants were followed from time of injury for a period of six or more months. The investigating team consisted of neurologists, psychiatrists, psychometrist, electroencephalographer, and social worker.

2. One hundred and two patients (51 per cent) complained of post-traumatic dizziness or vertigo at some time after the injury. Of this group 68 patients (34 per cent) complained of dizziness after hospital discharge, while 31 patients (16 per cent) were dizzy during hospital stay, but not thereafter. Eleven patients (6 per cent) complained of true vertigo at some time after injury.

3. Post-traumatic dizziness was always intermittent, and of variable duration, severity, and frequency. The outstanding precipitating factor was change in posture, whether sudden or otherwise.

4. Dizziness for longer than two months was characteristically associated with various factors of psychiatric significance—pre-traumatic nervousness, complicating environmental factors during convalescence, and to a less extent with immediate, abnormal, emotional reaction to the injury. These relationships point to the importance of psychological factors in the production or continuation of post-traumatic dizziness.

5. Severity of injury is significant in the production and continuation of post-traumatic dizziness as evidenced by the higher incidence of persistent episodes of dizziness in those patients who had prolonged coma, disorientation, or post-traumatic amnesia (over 12 hours). These relationships point to the significance of physical factors in the production and continuation of post-traumatic dizziness.

6. It is evident, therefore, that both physical and psychological factors

play an important role in the production of prolonged post-traumatic dizziness in the majority of cases.

7. Dizziness lasting for longer than two months was characteristically associated with headache and nervous symptoms (fears, anxieties, fatigue, and irritability). This association is a statistical reflection of the well known post-traumatic syndrome.

8. Vertigo, when present after trauma, was a much more persistent symptom than non-specific dizziness. There was a relationship between non-specific dizziness and true vertigo, for in some patients one could develop into the other.

9. Only 5 of 16 cases with bleeding from the ears had either dizziness or vertigo, an incidence which is lower than that for the group as a whole.

10. There was remarkably little evidence that post-traumatic dizziness is related to damage to the vestibular end-organ. In five cases of vertigo the initial signs pointed to damage to the brain stem, and it is considered possible that such may have been the focus of injury in many others. Even in the one case where vertigo followed bleeding from the ears with gross disorder of hearing, damage to the brain stem could not be excluded.

11. No reliable means was found for the differentiation of the lesser degrees of dizziness resulting from undoubted structural damage and dizziness associated solely with anxiety symptoms.

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EXANOPIC CENTRAL SCOTOMA, A PITFALL IN DIAGNOSIS

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ORDINARILY, amblyopia exanopsia is associated with strabismus. However, it may occur in patients who are not obviously cross-eyed. In either event, the loss of vision in one eye is associated with a central scotoma. In neurologic diagnosis a central scotoma in the field of vision of one eye usually indicates involvement of the optic nerve itself. Hence, a central scotoma that is really due to amblyopia exanopsia may prove to be misleading. Since this situation is not generally recognized, and especially since it is not mentioned in the authoritative work on perimetry by Traquair,[2] it is thought worth while to present the following case in illustration.

CASE REPORT

A twenty-four year old man was referred with the diagnosis of brain tumor. His complaint was severe headache for one and one-half months. Five years previously he had been in an automobile accident and had been unconscious for one minute but had no persistent symptoms. Two and one-half years before admission he suddenly noticed blurring of vision in the right eye whenever he looked at a target, and this condition persisted unchanged, so that he began sighting with his left eye. Seven months previously, while reading, he had severe headache,which was promptly relieved by glasses. Since then he had had occasional mild headaches. For six weeks prior to admission he suffered severe, persistent, right-sided headache. This headache was maximal in the right frontal region and seemed to extend backward. It was exacerbated by straining or jarring. Recently he had had episodes of feeling faint, especially on standing upright or on bending his head forward, and once he had lost consciousness momentarily.

Clinical examination revealed bilateral acutely choked discs, tenderness over the anterior part of the right temporal fossa, a central scotoma in the right eye on the confrontation test, and a pulse rate of 52. Roentgenograms of the skull revealed erosion of the floor of the sella, and displacement of the pineal body backward and to the left.

The working diagnosis at this time was probable meningioma of the right sphenoidal ridge. However, ophthalmic examination revealed that the visual acuity of the right eye without glasses was 5/200 and with a plus 6.00 sphere was 20/100. The left eye had no error of refraction and had a visual acuity of 20/15. There was bilateral papilledema of 4 diopters with one small recent hemorrhage at the edge of each disc. The blind spots were enlarged. Otherwise the visual fields were normal except for a central scotoma, 3 or 4 degrees in diameter, in the right field, which was revealed only by the 1 mm. and 3 mm. test objects at a distance of two meters with the plus 6.00 correction in place. In view of the marked degree of hyperopia in the right eye as well as emmetropia in the left, the central scotoma was considered to be due to amblyopia exanopsia rather than to involvement of the optic nerve. What was apparently a large central scotoma on the confrontation test was actually a small central scotoma associated with marked blurring of near vision due to the marked degree of farsightedness.

Therefore, the diagnosis was revised to: increased intracranial pressure due to right supratentorial lesion, probably subdural hematoma. An extracerebral process, subdural hematoma, was considered likely because of the relatively great lateral displacement of the

pineal body in the absence of hemiplegia or hemianopsia. Accordingly, burr holes were placed over the parietal bosses to explore for subdural hematomata, and, in the event of negative exploration, to allow for ventriculography. A very large liquid subdural hematoma was found on the right side and was drained. Subsequent roentgenograms revealed air at the site of the evacuated hematoma which extended widely over the frontal, parietal, and temporal lobes. The postoperative course was uneventful. The patient's headaches were relieved and the pineal body returned to the mid-line in six days. At this time ophthalmic re-examination revealed no change from the pre-operative status, except slight diminution in the degree of choking of the optic discs. Subsequently the patient became free of symptoms, and the papilledema disappeared. He was sent back to full military duty.

Re-examination was carried out six months later because of discomfort in the right frontal region. The examination of the eyes and nervous system revealed no change. The scalp was depressed over the burr holes; spinal fluid was normal in every respect; encephalogram revealed minimal enlargement of the lateral ventricles without deformity or displacement. The fourth ventricle was normal in size, shape and position. Cortical markings were normal on both sides. The patient resumed military duty free from symptoms.

DISCUSSION

As is generally known, disparity of the retinal images produced by the two eyes results in the suppression of one image. When such suppression occurs continually in one eye in early life, there results a diminution of visual acuity in that eye, so-called amblyopia exanopsia. What is not generally known is that such loss of vision is due to a small central scotoma, usually with a radius of about three degrees.[1] As in other defects of vision in one eye, the patient may become aware of his defect suddenly in adult life. In cases of obvious strabismus there is usually no difficulty in diagnosis. In other cases, careful study of the extra-ocular muscles and refraction will be required. The recognition of the nature of the central scotoma in this case was essential for its proper neurosurgical management.

SUMMARY

The central scotoma associated with amblyopia due to an error of refraction should be recognized as such, and not confused with that due to involvement of the optic nerve. An illustrative case is presented.

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NERVE GRAFTS: THE IMPORTANCE OF AN ADEQUATE BLOOD SUPPLY*

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THE USE of nerve grafts to bridge gaps is unavoidable in those instances in which the various manipulative measures for closing defects, such as the mobilization, rerouting or postural shortening of nerves with subsequent stretching, are insufficient or inadvisable. The use of autologous grafts, such as those employed by Bunnell[2] for the repair of nerves of the hand and by Ballance and Duel[1] for bridging gaps in the facial nerve within the Fallopian canal, has been successful in a high percentage of cases.[4] However, clinical success has been relatively uncommon following the insertion of grafts into gaps of other large major nerves. This occasionally led to the performance of end-to-end suture of nerves under great tension, in which cases the use of grafts might have proven wiser. This point was forcefully illustrated in a recent experience in which occasions arose for suturing the digital nerve of the index finger in two patients. In one, a male aged 65 years, loss of sensation over the radial border of the index finger followed a laceration at the base of the digit. Because of the presence of intense pain at the site of the scar, operation was undertaken. The nerve ends were found to be separated by a gap of 0.5 cm. and, after the terminal neuromas were resected, a graft 1 cm. long taken from the lateral femoral cutaneous nerve was introduced into the defect of the digital nerve and sutured with 10 drops of autologous unmodified plasma. Excellent coaptation of nerves was obtained. The operation was done 6 months after the original injury was sustained. Four weeks after the operation, sensation for pin prick had returned over the formerly analgesic area of the index finger. The day after this operation was performed, the occasion arose for treating a laceration of the index finger in a physician 31 years of age. The injury severed the branch of the median nerve at the base of the proximal phalanx on its radial side, exactly the same site as in the previous case. The patient, a pianist, was greatly concerned over the analgesia of the radial side of his finger. At operation 6 hours after the accident, direct end-to-end suture of the nerve was done by the combined tantalum wire-plasma clot technique using 6 drops of autologous unmodified plasma. The union appeared quite satisfactory except that it was under considerable strain. Examinations 4 weeks and again 7 weeks after operation revealed no return of sensation to the finger. The use

* This work was done under a contract recommended by the Committee on Medical Research between the Office of Scientific Research and Development and the Jewish Hospital of Brooklyn. The work was also aided by grants from the Committee on Medical Research of the American Medical Association and from the Dazian Foundation.

of a nerve graft rather than direct suture under tension would probably have been the operation of choice in this as in the former case.

A similar conclusion follows from our experience in dogs in which after the excision of 3-cm. segments of the sciatic nerve bilaterally, a 3-cm. fresh autologous sciatic nerve graft was used on one side and on the other side the nerve ends were sutured directly under considerable tension. Roentgenographic studies in two such cases following the intravascular injection of a mixture of red lead and glue showed good vascularization of the nerve on the side of the graft but practically none distal to the suture site on the other side (Fig. 1 A, B). Histological examination of the nerve specimens revealed considerably more fibrosis at the junction on the side of the simple end-to-end suture under tension. In another animal in which this procedure was carried out, there was regeneration of nerve fibers which had become myelinated down to the paw. However, fewer nerve fibers were present on the side sutured under tension. In two other dogs in which the same procedure was carried out, there occurred separation of the nerve ends on the side of the strained suture. Under such conditions it seems fair to conclude that nerve grafts would have a definite usefulness if the conditions governing their success could be determined, and this has been the purpose of our study.

FIXED AND FRESH GRAFTS

Some success has been reported with the use of formalinized homologous nerve grafts in humans[10,12] although evaluation of these results is difficult because of insufficient data. We have found, however, that satisfactory restoration of function may follow the use of formalinized nerve grafts in dogs but, on the whole, animal experimentation has shown[13] that the results obtained with such grafts and also with heterologous grafts are not as good as those which follow the insertion of fresh homologous nerve grafts. Autologous nerve grafts have been attended by better results, but in the case of the principal limb nerves the use of a single autologous nerve graft would be out of the question since there would be no justification in man for sacrificing one major functioning nerve for another. The only type of autologous nerve graft that could be used to bridge a gap in a large nerve is the cable graft prepared by placing segments of small nerves that can be sacrificed without serious deficit to the patient side by side until their combined cross-sectional diameter is equal to that of the nerve to be repaired. In our earlier experiments in dogs and monkeys the use of cable grafts prepared from intercostal nerves to repair defects in the sciatic nerve did not seem promising, since microscopically a large part of the central stump proved to be in contact with the considerable amount of connective tissue derived from the epineurium of the individual strands forming the graft. It seemed to us that such a condition would hinder the downgrowth of a significant proportion of nerve fibers from the proximal stump and our experiments at this point were focussed on the use of single grafts. The most favorable type of single graft that would be available for the repair of defects of the large nerves in

man is the homologous cadaver graft. There are good grounds for the belief that Schwann cells of the graft proliferate and guide the regenerating axis cylinders and are essential for satisfactory regeneration.[13] Hence it seems desirable that the graft be viable.

THICK GRAFTS

The use of fresh homografts in dogs is accompanied within the first 2 to 3 weeks by a variable, usually slight lymphocytic and monocytic response. At times practically no inflammatory reaction is discernible. The graft becomes invaded by macrophages which remove the myelin and axonal remains. The proliferation of Schwann cells and the disintegration of nerve fibers proceed in a manner similar to that in the peripheral stump. The grafts are capable of becoming innervated, conducting nerve fibers to the peripheral stump and, in favorable cases, good functional recovery may follow. However, not infrequently there occurred large patches of necrosis within the graft, usually in its center, or marked resorption and fibrosis without restoration of limb function. Complete absorption occurred in 8 of 50 fresh homografts* in 33 dogs which were followed 35 to 489 days after operation. Thinning of the graft of about 50 per cent occurred in 20 of the homografts, the degree of reduction in calibre of the nerve being approximately 30 per cent in the remaining grafts. Seven homografts, which had been kept in sponges soaked in serum for 24 hours, were removed at sacrifice of the dogs 64 to 195 days after operation. Three of these grafts showed a decrease in diameter of 50 to 75 per cent, the other grafts exhibiting less change in calibre. Five homografts stored in serum for 48 hours were removed from dogs 63 to 234 days following operation. There was reduction in calibre of the graft to the extent of 50 per cent in 2 grafts with less diminution in size in the other instances. Two of these animals, followed 228 and 234 days after operation, had shown an excellent functional recovery. In one dog a homograft kept in serum for 72 hours was used, and at sacrifice there was but about 30 per cent reduction in calibre of the graft. The decrease in size of the grafts refers to the approximate degree of reduction in calibre of the total number of nerve bundles. Blood compatibility was considered to be of possible importance in governing the fate of homografts but destruction and fibrous tissue replacement of grafts was found to occur even when preliminary cross-matching of the cells and serum of host and donor bloods showed no agglutination. The inconstancy of the histological and functional results associated with homografts led us to consider the possible significance of tissue compatibility, other than as expressed by cross-matching of blood, in determining the outcome following these operations. However, in one instance in which an autologous sciatic nerve graft was used to bridge a defect in a dog's sciatic nerve, examination of the graft 156 days after operation revealed reduction in its diameter to the extent of approximately 75 per cent and much of the graft

* Grafts present in infected wounds were discarded from all series.

had undergone fibrous tissue replacement. In fact complete absorption of the graft occurred in 4 of 50 autografts in 33 dogs followed for periods ranging from 33 to 380 days after operation. A reduction in calibre of the graft of about 50 per cent occurred in 3 grafts, the diminution appearing to be less than this in the remaining dogs. This experience seemed to indicate that some factor other than tissue compatibility plays the major role in the fate of a nerve graft.

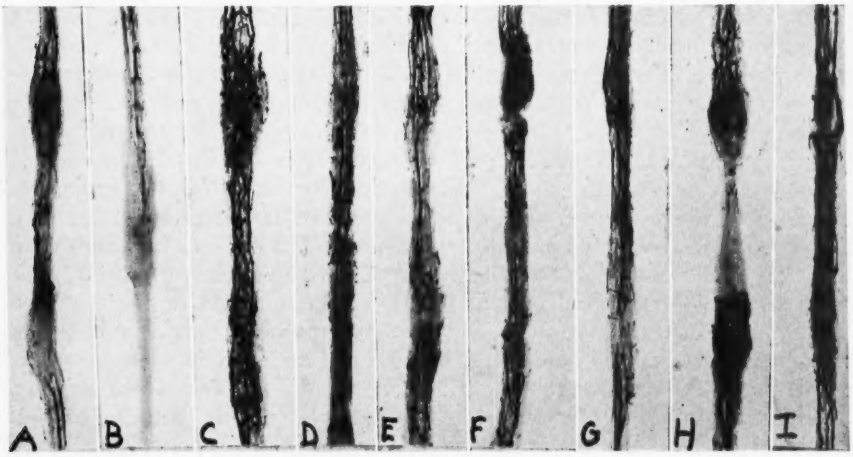

FIG. 1. Contact prints from x-ray films of sciatic nerves of dogs in which a mixture of red lead and glue was injected intraarterially. Autologous sciatic nerve grafts 3 cm. long were used in all instances and sutured by the combined silk-autologous plasma clot technique. A, Well-vascularized graft. B, Opposite sciatic nerve of the same dog in which, following excision of a 3-cm. segment, the nerve ends were sutured directly under tension. Note the virtual absence of injected blood vessels in the distal segment.* The injection was done 50 days after operation. C, Well-vascularized graft 26 days after operation. D, E, Grafts to which fat-areolar tissue flaps were sutured. Eleven days after operation the flaps were completely freed from the nerve graft on one side, just before the animal was sacrificed and injected. Note decrease in vascularization of the graft on the freed side (E). F, Graft to which a fat-areolar tissue flap was applied 11 days before operation, when ligatures were tied around the suture sites, thus cutting off longitudinally coursing vessels. The graft remained well-vascularized, an indication that it receives a rich vascular supply from the surrounding tissues. G, Graft to which a fat-areolar tissue flap was sutured. The flap was completely freed from the graft 19 days after operation, just before sacrifice and injection of animal. No decrease in blood supply of the freed graft is apparent, indicating that a free anastomosis between longitudinal and regional blood vessels has already been established. H, Graft surrounded by tantalum foil. The animal was sacrificed and injected 15 days after operation. Note sparseness of vascularization of the graft in zone of tantalum wrapper. I, Well-vascularized graft 15 days after operation.

* The relative avascularity of the distal segment of the nerve is of interest in relation to the observations of Highet and Sanders (The effects of stretching nerves after suture. *Brit. J. Surg.*, 1943, *30*: 355–369). They resected 2.5 to 4.0 cm. of the external popliteal nerve in dogs and performed end-to-end suture of the nerve with the limb in the flexed position. Following extension of the limb, considerable histological damage to the nerve occurred, the stretching force having fallen more heavily on the distal segment. "Adhesions cause the suture site to act as a fixed point, so that when the suture line is made close to a joint, the peripheral stump is subjected to greater tension than the central." In their experiments, rapid stretching did not appear to cause any more damage than slow stretching (over a period of 14 days) except that separation at the suture line occurred more frequently.

METHOD OF STUDYING VASCULARIZATION OF GRAFTS AND TECHNIQUE OF SUTURE

In order to test the importance of the vascular supply of nerve grafts in governing their take, studies were undertaken in dogs to determine the manner of revascularization of nerve grafts and then attempts were made to improve their vascular supply by the application of pedicled muscle or fat-areolar tissue flaps to them. The blood vessels were studied by histological methods as well as radiographically following the intravascular injection of a mixture of red lead and glue. This latter technique was elaborated by one of us (J. A. E.)[5] and consists of the injection of the mixture directly into the abdominal aorta. The red color of the injection medium facilitates gross dissection of the blood vessels and x-rays reveal the blood supply with considerable clarity (Fig. 1). The small capillaries of the nerves were rarely penetrated by the injection mass but these were studied in microscopical preparations. By these combined methods adequate studies of the blood supply of nerve grafts can be made.*

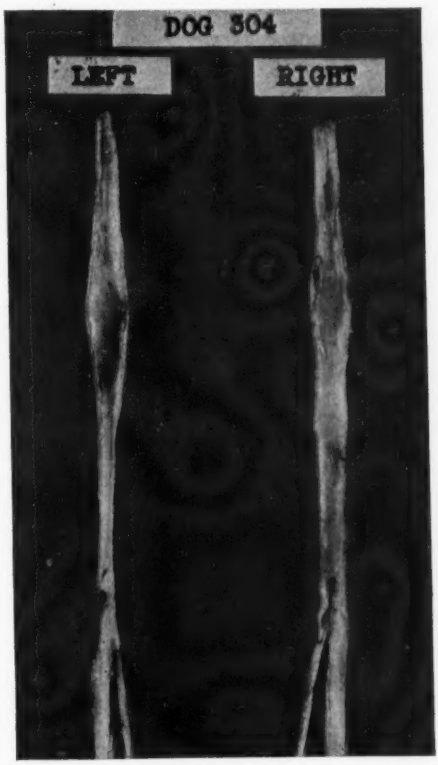

FIG. 2. Sciatic nerves of a dog in which grafts 3 cm. long were fixed in place with autologous unmodified plasma. An autograft on the right side was compared with a homograft removed from a cadaver about 1 hour post mortem and kept in a sponge soaked in homologous serum for 48 hours. The autograft appears about twice the size of the homograft but this is due partly to its greater connective-tissue capsulation. Cross-sections at various levels through the nerves stained with osmic acid for myelin sheaths show relatively little difference in the number of nerve fibers on the two sides. The slight difference was, however, in favor of the autograft. Excellent functional recovery occurred bilaterally in this animal sacrificed 228 days after operation.

Homologous nerve grafts, removed from the cadaver within 2 hours post mortem and kept in a sponge soaked in autologous serum or in Ringer's solution at room temperature for

* Some of the operations and injections were done by Dr. F. Kantrowitz, to whom the authors are grateful.

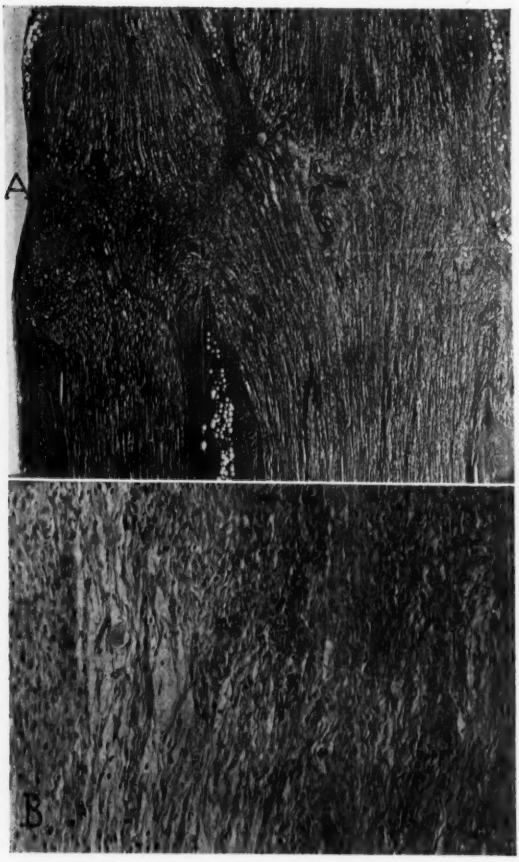

FIG. 3. A, Proximal suture site of a fresh cadaver nerve graft 3 cm. long 10 days after suture by the combined tantalum wire-autologous plasma clot technique. Blood vessels may be seen proliferating into the graft (below suture site) from the host stump. Hematoxylin and eosin, ×60. B, Proximal suture site of autologous graft 57 days after suture by the same technique. Practically no inflammatory reaction is seen at the suture site and nerve fibers pursue a fairly straight course. Hematoxylin and eosin, ×100.

periods up to 4 hours, as well as autologous grafts were used in our experiments. The success of a nerve graft depends to a large extent on the accuracy with which the ends of the graft are brought into apposition with those of the central and distal stumps. Since more precise contact of nerve ends with less trauma to them may be obtained with plasma clot than with the conventional thread suture, all nerve junctions were secured by the technique of autologous plasma clot (Figs. 2, 3 and 4). When some degree of strain existed at the suture site, then tantalum wire or silk tension sutures were used in addition to the plasma clot.[15] The grafts were obtained from the sciatic nerve and were thick enough to cover the transverse area of the host stumps. Unless this is done some of the nerve fibers from the central stump having no path along which to grow may be lost in the tissue surrounding the graft.

THE MANNER OF REVASCULARIZATION OF NERVE GRAFTS

As early as 3 to 4 days after introduction of the nerve graft, either autologous or fresh homologous, endothelial-lined blood vessels appear at the ends of the graft adjacent to the stumps to which they have been sutured. At this time no intact blood vessels are seen elsewhere in the graft. Five days after the transplantation, the blood vessels that enter the graft from proximal and distal nerve stumps become more prominent and an occasional vessel from the epineurial sheath may be seen in the outermost portion of the adjacent nerve substance. The ingrowth of blood vessels from the surrounding tissues into the epineurium and thence into the nerve tissue of the graft is

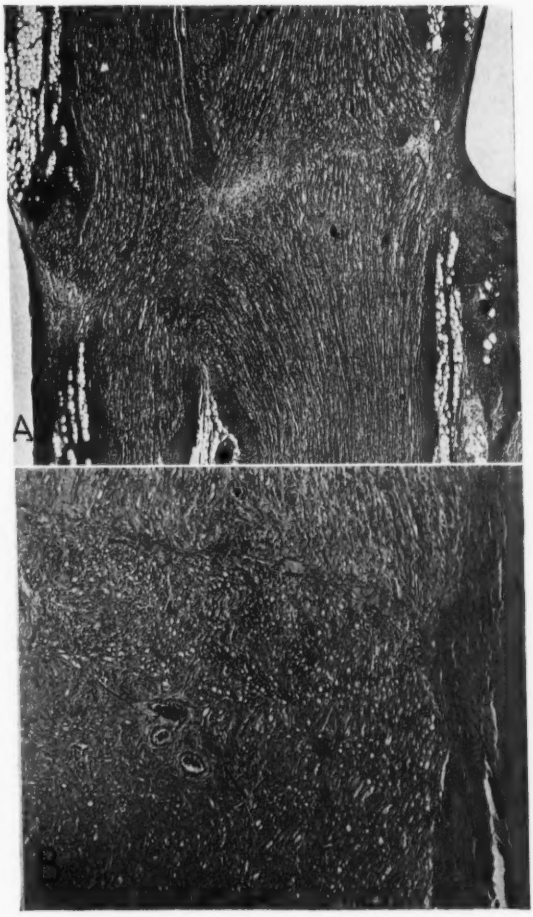

FIG. 4. A, Distal suture site of fresh cadaver nerve graft 4.5 cm. long 10 days after suture by the combined tantalum wire-autologous plasma clot technique. Practically no inflammatory reaction is seen at the suture site. Hematoxylin and eosin, ×60. B, Distal suture site of autologous nerve graft 3 cm. long 6 days after suture by the same technique. Note blood vessels growing into graft from host stump (shown in upper portion of photograph). Hematoxylin and eosin, ×50.

quite apparent 6 to 8 days after suture of the graft, and by this time further vascularization has developed at the graft ends (Figs. 3A and 4B). In these vascularized zones the cells of the graft are more numerous and stain more distinctly than elsewhere in the graft where the cells may be almost completely absent. A day or two later this manner of vascularization of the graft by the ingrowth of blood vessels from the nerve ends and also from the tissues around the graft is emphasized, and thrombosis of some of the blood vessels of the graft with recanalization of them becomes apparent (Fig. 5A). Some of the thin bundles of nerve fibers appear completely vascularized at this time, whereas the thick bundles show on cross section many blood vessels with intact cells peripherally and with few or no blood vessels and cells in the central portion of the graft. In other words, the blood vessels in the mid-segment of the graft enter it from the surrounding tissue and grow centralward. Other vessels which appear earlier are derived from the stumps of the host nerve and grow from the ends of the graft toward its mid-portion. Ten to 15 days after insertion of the nerve graft, an increase in the number of blood vessels occurs and further evidence of thrombosis and recanalization of them appears.

Myelophages are seen in the nerve graft and, like the normal cell constituents of the nerve, they occur first in those areas supplied with blood vessels and their subsequent appearance runs *pari passu* with the latter (Fig. 5 B, C). Approximately 3 weeks after their introduction grafts 3 cm. in length

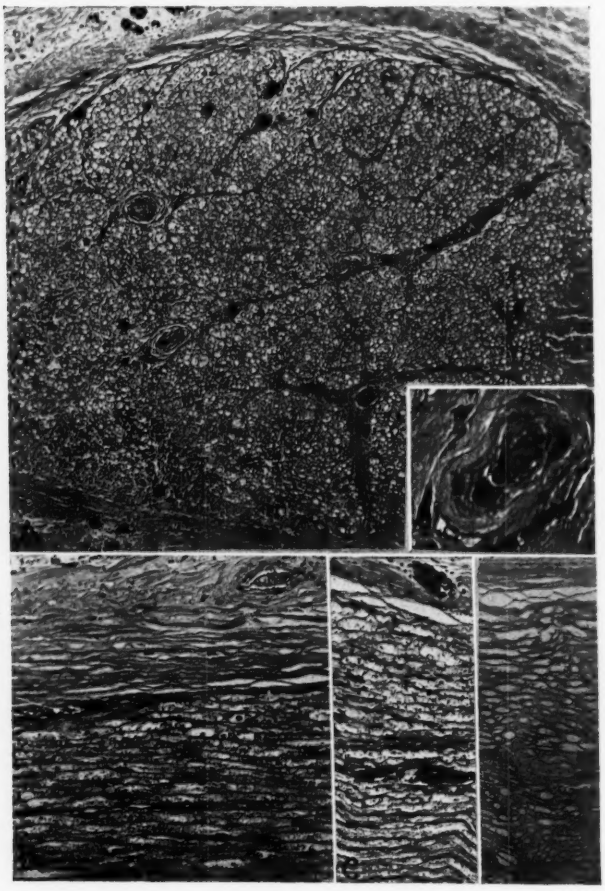

FIG. 5. A, Cross section through center of a 3-cm. sciatic nerve autograft 18 days after its insertion. Fairly good vascularization of the graft has occurred although some of the vessels are almost completely thrombosed (see insert). The injected red lead is visible in the vessels, few of which are in the stage of recanalization. A small necrotic area is on the right at the margin of the photograph. B, Section through autologous and C, through fresh cadaver graft 15 and 18 days after operation showing vascularization of the nerve sheath and periphery of the nerve bundle with intact cells, including myelophages, most numerous in the vascularized zones. D, Well-preserved cells in a cadaver nerve graft 3 days after its introduction. Blood vessels are not present at this stage. Sections stained with hematoxylin and eosin, A, ×60 (insert ×260); B, ×100; C, ×100; D, ×85.

may become well-vascularized (Fig. 1 C, I). The behaviour of fresh homologous cadaver grafts, kept in a sponge soaked in Ringer's solution at a temperature of 5°C up to 6 hours after death of the donor animal, is essentially the same as that of single autologous nerve grafts except that somewhat more inflammatory changes (infiltration with monocytes and lymphocytes) are apt to occur in the former. At times, however, no histological differences are discernible in the two types of grafts and no inflammatory reaction occurs.

During the period required for vascularization of the graft the cells of the non-vascularized portions of the graft, many of which appear quite intact for several days after its introduction (Fig. 5 D), probably absorb their nutrition from the surrounding tissue. Some portions of the graft undergo fibrosis over large areas (Figs. 6, 7 and 8), whereas other portions become richly supplied with blood vessels and innervated. Complete fibrosis of autologous and homologous grafts has been found and, in some instances,

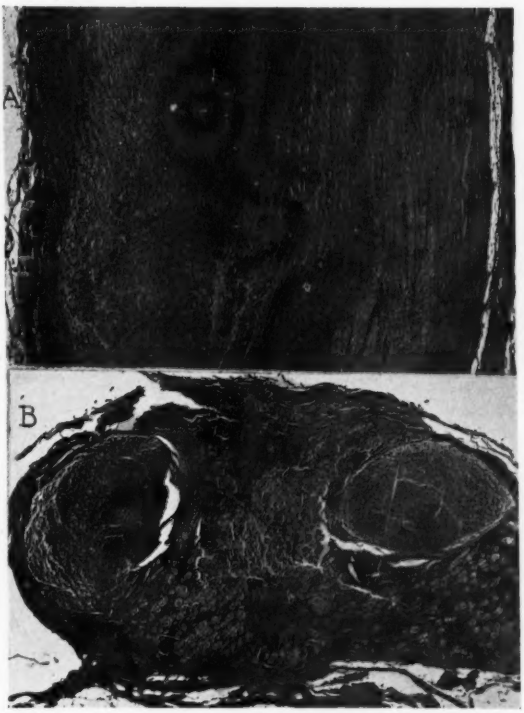

FIG. 6. A, Proximal suture site of fresh cadaver graft 3 cm. long sutured by the autologous plasma clot technique. Good functional recovery had occurred in this animal sacrificed 489 days after operation. Good longitudinal orientation of nerve fibers is present at the suture site and there is very little fibrosis. Hematoxylin and eosin, ×10. B, Cross section through center of same graft. Although satisfactory functional recovery of the hind limb had occurred, there was a considerable reduction in the number of nerve fibers within the graft. Note the many small bundles of nerve fibers within the fibrous-tissue matrix of the graft. The fibrosis is doubtless secondary to inadequate vascularization of the graft. This represents the usual or even rather above average appearance of a thick nerve graft. Although good restoration of limb function occurred in this animal, one wonders whether this degree of return of innervation in the human hand, with its much more complex function, would have proven at all satisfactory. Hematoxylin and eosin, ×27.

similar grafts on the other side of the same animal were well-vascularized and innervated. The variability in the histological and functional results of nerve grafts is probably largely dependent upon variations in their blood supply. In certain cases, the bed in which the nerve graft lay may be more favorable for the development of adequate vascularization than in others.

Following carefully performed suture of nerve grafts by means of the plasma clot technique slight fusiform enlargement of the proximal and distal suture lines has been found (Fig. 2). Microscopically very little connective tissue has been present at the junctures, no more distally than at the proximal suture site. Axis cylinders have been found to cross the suture lines and in well-made unions they pursue a fairly straight course into the trans-

plant, through the distal suture line and into the peripheral segment. Nerve fibers have been found to cross the proximal suture line as soon as 10 days after introduction of a graft and in a 5-week specimen they had traversed the distal suture site of a graft 3 cm. in length. Studies undertaken to determine the rate of growth of nerve fibers through grafts have not yet been completed but there seems to be no doubt from our observations and prior ones reported by Young, Holmes and Sanders[17] that the rate is not as fast as that following direct end-to-end suture of nerves.

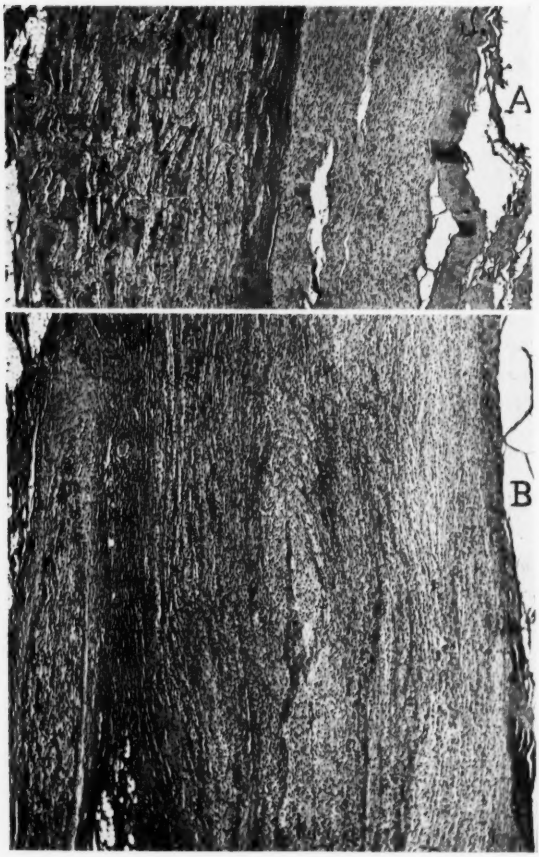

FIG. 7. A, Longitudinal section through cadaver graft shown in Fig. 6. On the right is a rather large bundle of well-preserved nerve fibers but on the left small bundles of nerve fibers traverse a connective-tissue matrix. Hematoxylin and eosin, ×35. B, Distal suture site of graft shown above. Less fibrosis is apparent than in the center of the graft. Hematoxylin and eosin, ×30.

THE PATTERN OF BLOOD VESSELS IN NERVE GRAFTS

Roentgenographic studies of transplanted sciatic nerves following the intravascular injection of a mixture of red lead and glue indicate that an important source of blood supply for grafts is their surrounding tissue. Blood vessels enter the graft from the host stumps a few days sooner than from the tissues around the graft and vascularization then proceeds from both sources. Within approximately 3 weeks a rich blood supply of the graft has developed (Fig. 1 C, I). At this time it may be seen roentgenographically, and confirmed by histological examination, that the blood vessels that traverse the suture sites, although they may be numerous, are usually small in contrast to the large vessels that enter the graft from the regional tissues. Even weeks after introduction of the nerve graft the principal longitudinal vessels often do not cross the junctions.

That the graft, within a period of a few weeks after its introduction into the recipient, is dependent for its vascular supply largely upon the surrounding tissues was demonstrated by the following experiment. Three-cm. segments of the sciatic nerve were excised, cross-switched and sutured by means of the combined silk-autologous plasma clot technique. In addition, the surrounding fat and areolar tissue was sutured to the scarified epineurium of the nerve graft in an attempt to improve the vascularization of the latter. The same procedure was carried out on both sides of the animal. Eleven days later both grafts of the animal were exposed and on one side the graft was freed from the surrounding tissue. On the next day x-ray studies following the intravascular injection of the radio-opaque medium revealed a striking contrast in vascularization of the grafts on the two sides, the graft freed from the surrounding tissue being to a large degree deprived of blood vessels (Fig. 1 D, E). This experiment was repeated after a post-operative period of 19 days, 26 days and at longer intervals with the result in these instances that practically no difference in vascularity was apparent on the two sides of the animals (Fig. 1 G). In other animals the initial operation was the same as that described but at the time of reoperation the junctions between the graft and host nerve were crushed by silk ligatures tightly applied on one side of the animal, the other limb serving as the control. Very little difference in the blood supply of the grafts on the two sides was apparent after x-ray studies were made for the visualization of blood vessels (Fig. 1 F), thus indicating that a rich vascular supply enters the graft from the surrounding tissues. It must be stated that the small capillaries that may be seen microscopically entering the nerve graft from the host stumps are not clearly visualized by the radiographic technique employed. They doubtless play an important role in the vascularization of the nerve graft. The relative importance of the blood

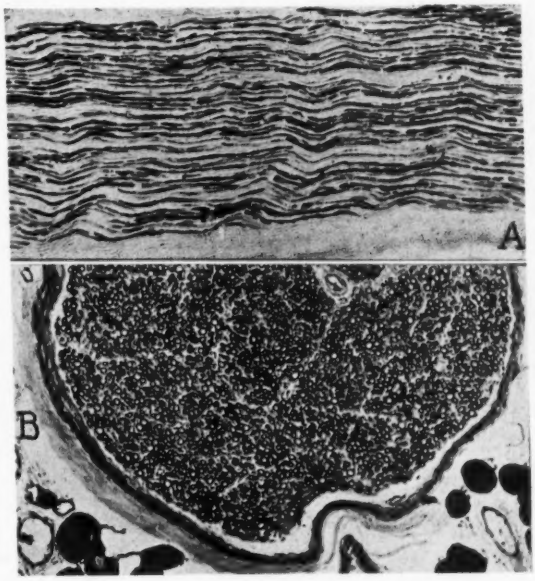

FIG. 8. A, Axis cylinders just above ankle in limb of animal in which graft shown in Fig. 7 was introduced. Good innervation has occurred. Gros-Bielschowsky impregnation, ×70. B, Myelinated nerve fibers at approximately the same level as in A. Osmic acid stain, ×100.

vessels entering the nerve graft from the surrounding tissue has been further tested by cross-switching 3-cm. segments of the sciatic nerve in 3 dogs and surrounding the graft on one side with tantalum foil. Very little vascularization of the graft under the tantalum foil occurs (Fig. 1 H), and in one instance complete necrosis of the graft under the foil was found 25 days after the operation. These experiments leave no doubt that the circulation of a nerve graft is derived to a large extent from blood vessels of the surrounding tissue. After a period of approximately 3 weeks a free anastomosis between the longitudinal and regional blood vessels develops (a condition that exists in the normal peripheral nerve), so that cutting off the blood supply from either source results in no diminution of the vascularization of the graft as demonstrated by the radiographic technique described.

The pattern of blood vessels of the nerve graft becomes similar to that of normal nerves. Several large blood vessels run longitudinally along the graft and here and there occur horizontal connecting offshoots which tend to produce a step-ladder effect. In addition there is a rich meshwork of small blood vessels running in various directions. The similarity of vascular pattern between normal nerves and nerve grafts suggests that revascularization of the latter may occur along the preexistent vascular channels. That this may actually be true is supported by the histological observations that blood vessels within the graft at times become thrombosed within the first few weeks after introduction of the graft and then recanalization of them may occur.

ATTEMPTS TO INCREASE THE VASCULARIZATION OF NERVE GRAFTS

Since the vascularization of nerve grafts seems to be one of the most important factors concerned in success following their use, various methods have been tried to improve the vascular supply of nerve grafts and thus prevent the resorption and fibrosis of them which sometimes occurs.

A. *The Use of Collodion Tubes for the Preparation of a Bed of Granulation Tissue for Nerve Grafts.* In an attempt to produce a well-vascularized bed for the reception of nerve grafts, tubes of collodion were inserted into defects in the sciatic nerve. The walls of the collodion tubes were 1 mm. thick, and contained 1 mm. perforations, 1 mm. apart. At intervals varying from 8 to 21 days after introduction of the tubes, the wounds were reopened and the collodion tubes removed. The tubes were found to be enveloped in a membrane of connective tissue and it was planned to place the nerve graft in this envelope at the time of reoperation to determine whether it would lead to greater vascularization of the graft than on the control side, where the excised segment of nerve was not replaced by a collodion tube. Eight such operations were carried out and the membrane that formed around the tube was found in each case to consist of a few layers of connective-tissue cells and fibers which formed its inner lining. Moderate numbers of blood vessels were observed under the fibroblastic layer. The vascularization of the tissue surrounding the collodion tube was not strikingly greater than on the

control side so that the procedure did not appear promising and these experiments were discontinued.

The occurrence of an infection around a nerve graft was found to be associated with a well-marked increase in vascularization of the distal stump in one instance. This finding led us to consider various methods of producing inflammation and thereby increasing the blood supply of nerve grafts. However, in other instances of inflammatory reactions of various grades, which usually were associated with infection, no increased vascularization of the nerve grafts was observed so that it was considered unwise to undertake experiments of this type.

B. *The Use of Pedicled Flaps of Fatty Areolar or Muscle Tissue Applied to Nerve Grafts.* The sciatic nerve lies in a bed of fatty and areolar tissue and the flaps were made by undercutting this layer at its lateral margins and then suturing the 2 flaps to the middle 1.5 cm. of the 3 cm. single autologous or fresh homologous cadaver-sciatic nerve graft. The sutures were carried through the scarified epineurium of the graft. In later experiments the undercutting procedure was omitted since it was believed that vascularization of the flaps might be impaired as a result of the severance of some of its blood vessels. The loose tissue on each side of the nerve was merely brought directly over the graft and sutured to it.

Our early experiments dealing with the application of pedicled muscle flaps fashioned from the biceps femoris muscle to the nerve grafts resulted occasionally in necrosis of the muscle flap and this was attributed to inadequate vascularization. Studies were then undertaken to determine the blood supply of this muscle and it was observed that the blood vessels are present mainly at its proximal and distal extremities. It then became possible to prepare a more favorable type of muscle flap for suture to the nerve graft. Since the biceps femoris runs fanwise from above downwards, it is possible to cut the flap mainly in the direction of its muscle fibers, with a broad base distally and its apex near the origin of the muscle. The large blood vessels may thus be avoided and the flap retains a rich vascular supply. The muscle flap is then sutured to the epineurium of the nerve graft with its raw surface applied to the latter. The pedicle of the muscle flap was cut long enough to preclude the possibility of tugging on the nerve graft as a result of muscle contraction.

The effect of the application of muscle or of fat-areolar tissue flaps to nerve grafts was studied in 30 dogs. Bilateral fresh homologous sciatic nerve cadaver grafts 3 cm. long were used to bridge defects following the excision of 2-cm. segments of the sciatic nerve in 11 dogs. In the remaining 19 dogs, 3-cm. segments of the nerve were excised and then cross-switched. Fat-areolar tissue flaps were applied unilaterally to the nerve grafts in 19 dogs and muscle flaps were sutured to one of the grafts in each of 11 dogs. In 22 of these animals, in which the survival period varied from 3 to 125 days, roentgenographic studies of the nerve were made following the injection of a mixture of red lead and glue. Also histological preparations of these nerves

were studied. In 4 of these animals the combined studies indicated better vascularization and less fibrosis of the grafts to which the flaps were applied. In 3 instances the graft was thinner and less vascularized on the side to which the flap was applied and in the remaining 15 dogs there was no difference whatever in the grafts on the two sides. The 8 remaining dogs of this series were observed for periods ranging from 164 to 321 days. Autologous cross-switch grafts were used in 5 of these animals and cadaver grafts in 3. There occurred complete absorption of one cadaver graft to which a muscle flap was applied, while the other cadaver graft lacking the flap showed a 50 per cent reduction in calibre. The other muscle flap in this series had been applied to an autologous graft and in this instance too the graft had undergone complete absorption while its fellow, to which no flap was applied, but which received many blood vessels *via* spontaneously formed adhesions to the surrounding tissue, was essentially unreduced in size. In the other 6 animals fat flaps were used and practically complete absorption of the grafts occurred in one of them. In 3 of these dogs the grafts were somewhat thicker on the side of the fat-areolar tissue flaps and in the remaining 2 dogs there was no difference in appearance of the grafts on the two sides. The muscle flaps in most instances had either become converted to fibrous tissue or had disappeared. These experiments indicate clearly the futility of attempting to improve the vascularization of nerve grafts by the use of flaps such as described.

C. Tunnelling Grafts Through Muscle. In a series of 6 dogs fresh homografts 4 to 5 cm. in length were introduced into sciatic nerve defects following excision of 2-cm. segments of the nerve. On one side of these animals the graft was placed in a muscle tunnel made by forcing a hemostat through the biceps femoris and enlarging the opening so that it would accommodate the nerve without constricting it. The middle 3-cm. segments of the grafts were thus in contact with raw-surfaced muscle which it was thought might favor vascularization of the graft. These animals were followed for periods of time ranging from 89 to 161 days after operation, when they were reoperated upon just before sacrifice. At reoperation the nerves were stimulated with faradic current at various levels above and below the graft and the muscle responses were compared on the two sides. Such tests yielded no striking differences in the two limbs of the animals. There was moderate thinning (30 to 50 per cent) of both grafts in 3 animals, more reduction in calibre of the tunnelled graft (50 as against 30 per cent) in 2 other dogs, and in the remaining dog the tunnelled graft was essentially unreduced in thickness while its fellow showed a thinning of about one third. Again the conclusion follows that the desired objective of preventing the reduction in calibre of grafts by tunnelling them through raw-surfaced muscle was not attained.

CABLE GRAFTS

Microscopic study of nerve grafts has shown that thin bundles of nerve become vascularized and innervated more readily than thick bundles and it was therefore decided to repeat our earlier experiments on the use of cable grafts. In these earlier studies autologous cable grafts were used, the strands

being taken from the intercostal nerves. Many strands (8 to 10) were required to form a cable the calibre of the dog's sciatic nerve and 4 cm. in length. The considerable amount of connective tissue derived from the epineurium and perineurium of the filaments of the cable was thought to be disadvantageous in that the downgrowth of axis cylinders from the central stump might be impeded. Moreover this procedure necessitated the excision of 5 to 6 intercostal nerves and the dogs and monkeys did not tolerate this operation well—the mortality rate was high. For these reasons, chiefly the second, it was decided to use cable grafts formed from thicker strands of dog cadaver nerve. The cable was formed from 4 to 5 strands of brachial nerves (twice or more as thick as the intercostal nerves). Only the ends of the cable were glued together with plasma, and the cable was made long enough so that the intervening segments could be spread about in the tissues to favor the development of vascularization. The cable grafts were 4 to 5 cm. in length and were sutured into defects resulting from the excision of 2 to 3 cm. of the sciatic nerve in dogs. This experiment was controlled against a single sciatic homograft removed from the same cadaver and introduced into the defect in the opposite sciatic nerve. The grafts were removed 1 to 3 hours post mortem and were kept in a sponge soaked in serum. They were used within 3 hours later except in two instances in which a period of 24 hours had elapsed before the grafts were sutured in place. These operations were done in 7 dogs. The animals were reoperated upon at periods varying from 65 to 180 days after introduction of the grafts. At reoperation faradic stimulation of the sciatic nerve at various levels was carried out and the muscle responses were compared on the two sides. The animals were then sacrificed and the nerves studied histologically.

Complete recovery from foot drop had occurred in 4 animals, in 2 of which the grafts had been stored in serum for 24 hours. No striking differences in gait* or in muscle responses following faradic stimulation were ob-

* Functional studies of recovery were carried out in most animals. These were done by Dr. Walter Bornstein. Position sense was tested by the ability of the animal to correct an upside-down position of the foot. Touch sensation was tested by thrusting the animal's foot over the edge of the table to determine whether the foot would be returned to its original position, the placing reaction described by Rademaker and by Bard (*Macleod's Physiology in modern medicine.* P. Bard, Ed. St. Louis: C. V. Mosby Co., 1938, 8th ed., p. 148). Pain sense was tested by pin-prick or by pinching the foot and following the progressive recession of the zone of anesthesia. Motor functions were studied by observing the animal's gait and posture. The presence of foot drop, the result of paralysis of the extensors of the foot, was considered to be one of the most important signs following section of the sciatic nerve. An attempt was made to evoke foot drop under as many different conditions as possible, as, for example, by allowing the animals to walk on a slippery floor, or incline, upstairs and downstairs and by suddenly stopping or turning the running animal. Paresis of the plantar flexors of the foot resulted in an inability of the animal to raise the heel on the affected side so that the animal stood or walked on the whole sole of his foot rather than on his toes. In several animals there was found gross discrepancy between the results of these functional studies and the observations at autopsy. Recovery from foot drop was recorded in animals in which autopsy revealed practically complete absorption of the nerve graft and in which the muscles of the foot could not have become reinnervated. In such instances synergic muscles must have assumed the function of the extensor muscles of the foot and given the appearance of recovery of function of these muscles when such recovery had in fact not taken place. The conclusions based on the functional tests described were considered tentative until checked by histological studies to determine the extent of regeneration. These studies are still in progress.

served on the two sides of these animals. It must be stated that the comparisons of muscle movements, following application of the electrical current to the nerves, were of a crude sort consisting merely of visual observation of the extent of contraction of various parts of the limb.

At autopsy the individual strands of the cable graft were found to have become agglomerated into a cord rather resembling the single graft. In some instances, however, the segments of cable graft were grossly identifiable. Microscopically the strands proved to be embedded in a vascular connective-tissue matrix.

In one dog complete absorption of the single graft had occurred while the cable graft was essentially unreduced in size. Microscopically very little fibrosis of the strands was evident. In 3 of the remaining 6 dogs histological preparations revealed more fibrous-tissue replacement of the single grafts with fewer nerve fibers within them, the condition being reversed, however, in the other 3 animals. Axis cylinders were found to have grown through the grafts to the end of the nerve and medullation had taken place. Actual counts of nerve fibers have not yet been made but osmic acid preparations through various levels of the two types of grafts revealed no consistent differences. Although the results in this small series of experiments are somewhat better with the cable grafts, their superiority is certainly not striking.

All homografts used after 3 hours post mortem were kept at a temperature of approximately 5°C either in a sponge soaked in serum or immersed in test-tubes containing serum. These conditions were considered suitable for maintaining the viability of nerves as a result of some experiments carried out with Dr. Lorente de Nó at the Rockefeller Institute. The ability of nerves to transmit impulses was employed as an index of their viability and hence their suitability as nerve grafts. On the basis of these studies it seemed that homologous serum is superior to either Ringer's or normal saline solution as a medium for preserving the viability of fresh cadaver nerves and that a temperature of approximately 5°C is preferable to room temperature. The receptacle in which the graft is kept is loosely stoppered so that air might enter in order to supply the nerve with its necessary oxygen requirement.

DISCUSSION

The incidence of complete absorption of sciatic nerve grafts was found to be approximately twice as high with fresh homografts as with autografts, i.e., 16 per cent as against 8 per cent. Also the degree of reduction in calibre of nerve at the expense of a loss of nerve fibers is apt to be somewhat greater with homografts. It is of interest, however, that of 13 stored homografts, which were kept in serum for periods of time varying from 24 to 72 hours, complete absorption did not occur in a single instance and, in general, the degree of thinning of the graft was rather moderate. Complete recovery of function took place in 2 dogs with 48-hour-old homografts. This experience seems confirmatory of that of Gutmann and Sanders[6] that "stored homografts gave a distinctly better recovery than fresh homografts. . . . " These

authors stored the grafts in Ringer's solution. The better degree of recovery following stored homografts was considered to result from the reduction of the undesirable cell reactions brought about by storage. The degree of recovery obtained by Gutmann and Sanders "after stored homografts was definitely superior to that obtained after fresh homografts, although slightly inferior to the results of autografts and sutures." Our results are in agreement with this statement and would seem to favor the use of stored rather than fresh homografts. However, further work seems indicated to test this point.

In some instances at autopsy the grafts have been found encapsulated in a fibrous tissue envelope. Sanders and Young[13] have found this tendency toward capsulation of the graft in rabbits greater in the case of fresh homografts than with stored homografts or with autografts. Our results in dogs appear inconclusive on this point. Adhesions between the nerve graft and its bed occurred in all cases. This would appear desirable since the necessity for blood vessels to enter the graft from the surrounding tissues during its early period in the host has been indicated by the results of our experiments. Such a condition might, however, conceivably lead later to delay in functional recovery as a result of interference with the free mobility of the nerve and the exertion of tension upon it coincident with movement of the part. If this does occur, then reoperation with freeing of the graft from its adhesions to the surrounding tissue and even transposition of it to a relatively unscarred bed, if possible, might be advisable. Injection experiments with red lead and glue in dogs following separation of the graft from its neighboring tissue has indicated that a free anastomosis develops between the longitudinal and regional blood vessels in approximately 3 weeks. At this time then, or preferably several weeks later, separation of the regional vessels from the graft would probably do no harm and might hasten restoration of function to the innervated part. However, this supposition remains to be tested. Such a neurolysis might be justifiable clinically under conditions where, after months or a year or longer, recovery has either not occurred or has failed to reach a satisfactory level.

The extent of functional recovery following the use of sciatic nerve grafts in dogs has varied and it seems likely that the extent of the vascularization of the graft represents the most variable factor involved. It has been shown that the vascularization of nerve grafts proceeds from two sources: (1) the host stumps and (2), the bed in which the nerve graft is placed. With very short grafts it is possible that adequate vascularization may be derived from the nerve stumps within a short time and satisfactory regeneration follow. In fact, rapid vascularization with very little fibrosis of grafts 5 to 7 mm. long has been found to occur in dogs. However, such grafts are hardly ever of practical value and with grafts several cm. long satisfactory vascularization from the nerve stumps cannot be expected to take place. Without blood vessels entering the graft from the surrounding tissue the mid-portion of these grafts would surely undergo necrosis with subsequent fibrosis and in-

terference with the downgrowth of nerve fibers. In view of this fact the use of impermeable membranes, either of animal or metallic origin, to enwrap the nerve for the purpose of "protecting" it is to be condemned. This practice prevents the ingrowth of blood vessels to the graft from the surrounding tissue and massive necrosis may follow.

Revascularization of a sciatic nerve graft 3 cm. in length in a dog requires approximately 3 weeks. During this period some of the cells become pale, pyknotic and disappear and the architectural pattern of the nerve graft becomes indistinct. Such changes become more marked near the center of the graft where small areas of necrosis tend to occur. The occurrence of some degree of necrosis and fibrosis in grafts together with the fact that two suture lines are present when they are used, renders conditions for functional restoration less favorable than in the case of direct end-to-end suture of nerves. But when the latter procedure cannot be done without great strain at the suture line, then the use of a nerve graft is in order. Very satisfactory recovery of function may follow the use of 3-cm. cadaver grafts in dogs and it is unnecessary to resect the distal suture line in cases where accurate coaptation of the graft with the host stumps has been obtained and the junctions made secure by means of autologous plasma clot suture with or without the aid of silk or tantalum wire tension sutures.

Within the first few days after introduction of a graft, before blood vessels have entered it, the cells of the graft (many of them do survive) probably derive their nutrition by the process of osmosis from the surrounding tissue. Further evidence that a part of the graft remains viable is the observation that there occurs thrombosis of some of its blood vessels with recanalization later. With the entrance of blood vessels into the graft, its cells multiply and large phagocytic cells (myelophages) make their appearance with the newly formed blood vessels. Less necrosis occurs in thin than in thick grafts because of the more rapid vascularization of the former and it is for this reason that cable grafts would appear to be more promising than single thick grafts for the repair of defects in nerves of large calibre.[3] However, with the use of cable grafts a certain number of downgrowing axis cylinders from the central stump encounter epineurium and perineurium derived from the individual strands of the cable and many of these fibers become lost from the functional standpoint. On the other hand, with single thick grafts many of the nerve fibers are doubtless obstructed by areas of necrosis and subsequent fibrosis of the graft resulting from inadequate vascularization. These changes develop to some extent in all grafts but are more marked in thick ones. They occur in the center of the graft, that is, in those areas that are remote from the sources of its blood supply. Some degree of sacrifice of the proliferating axis cylinders seems inevitable in either case. In those instances where minimal necrotic and fibrotic changes take place in thick grafts the microscopical appearance of the graft is very favorable, the number of downgrowing nerve fibers, which become myelinated, is plentiful and the functional result in the dog is excellent and was not bettered in our experiments by the use of the ca-

ble graft. However, it seems that the risk of absorption is somewhat greater with the single graft which would tend to favor use of the cable graft. The use of thick (cadaver) grafts would appear to present an advantage in that one can choose a homologous nerve (sciatic nerve graft for repair of a gap in the sciatic nerve) taken, in fact, from the same level of the nerve. Thereby one can to some extent at least match fasciculi of the graft and the host stumps in a rough way. However, as an actual fact, much distortion of the internal relationships occurs within the graft as a result of its nerve fiber degeneration and fibrous proliferation so that the theoretical advantage is thereby largely negated.

The use of single thin grafts for the repair of defects in the digital nerves is associated with satisfactory results but clinical experience with single thick grafts has been disappointing. If single thick grafts (usually obtained from cadavers or amputation stumps) are used, it seems wise to split the graft longitudinally into several bundles or more if this can be done easily and without significant trauma to the nerve. This suggestion was first made to us by Lt. Commander T. I. Hoen. The procedure combines the advantages of the more unobstructed suture line of a single graft with the thinner, more readily vascularized intermediate segments of the cable graft. However, this plan cannot always be followed since the bundles of fibers within a nerve do not regularly pursue a parallel course but may be interwoven so that separation of the graft into bundles would, in these instances, result in the severance of a large number of nerve fibers with subsequent misdirection of many axis cylinders into the surrounding connective tissue. If the bundles of a single thick nerve graft are loosely connected and are easily separable, this measure should be taken and the strands spread apart in the bed of the graft.

The use of cable grafts seems somewhat preferable to single grafts for the repair of defects in large nerves for two reasons: firstly, the thin strands of nerve appear to be more readily vascularized than the thick single graft, and secondly, autologous nerves can be obtained for the purpose of forming the cable grafts and the possibility for a favorable take is greater with an autologous than a homologous nerve graft. However, some degree of necrosis and fibrosis appears inevitable with all grafts. For this reason the functional results following the use of grafts for the repair of defects in the major nerves cannot be expected to equal those associated with direct end-to-end suture of nerves. The loss of nerve fibers in transit through the graft or their deflection by barriers of fibrous tissue is considerable except, probably, when very thin grafts are used. In some cases in which it becomes possible to join nerve ends directly after rerouting a nerve and acutely flexing a neighboring joint, some degree of damage to the nerve follows the subsequent gradual extension of the joint and stretching of the nerve.[8] The results in some such cases after extensive resections (10 cm. or more of the lateral popliteal nerve) have been a complete failure[8] and it is possible that the use of nerve grafts under such conditions might be preferable. However, the clinical results in many cases where less extensive resection is necessary appear to be better

than one might anticipate if nerve grafts were used. Satisfactory return of function to the hind limb has followed the introduction of grafts into sciatic nerve defects in dogs in spite of the great reduction in the number of nerve fibers that follows. A similar gratifying recovery may occur with the repair by grafts of defects in some of the nerves in humans. However, repair of the ulnar or median nerve by operations involving the use of grafts is not likely to be so satisfactory. These nerves contain a great number of small funiculi supplying muscles that carry out delicate and complex functions. Misdirection of axis cylinders and reduction of their number in passage through a thick graft occur in spite of the branching of axis cylinders from the central stump that accompanies regeneration. This would probably impair considerably the range of movements and the accuracy of proprioceptive sensation required for precise coordinative activity. However, grafts should be used only when methods of achieving end-to-end union of nerves are impossible or inadvisable and, under such conditions, they are worthy of trial.

When cable grafts are used, a natural question is the optimal calibre of the strands that should be used to form the cable. If the decision is made to use an autologous graft, then one will be obliged to choose cutaneous or possibly intercostal nerves or both, depending on the nerve to be repaired and the size of the defect. If the less desirable choice of a cadaver nerve is made, then one has the option of selecting a nerve from a greater range of sizes. The fewer the strands comprising the graft, the less the obstruction of nerve fibers at the suture site but the greater the likelihood of their blockage by the fibrotic areas developing within the thick strands of the graft. On the other hand, if thinner nerves are used, more strands will be required to form a cable the calibre of the nerve to be repaired and greater hindrance to the nerve fibers at the suture site will be offered by the connective-tissue sheaths of the individual filaments. But there will be less possibility that within the thin strands of the graft fibrosis will appear with impedance to the downgrowing axis cylinders as a result. Some degree of compromise is necessary in the selection of the calibre of the nerve to be used for the graft and it is difficult to know just where the happy medium lies. For the repair of the dog's sciatic 4 to 5 strands were used and necrosis within some of the segments of the graft occurred. It seems, then, that thinner strands might be preferable for a nerve the size of a dog's sciatic—6 to 8 strands rather than 4 to 5 would probably be more desirable from the standpoint of minimizing the fibrosis and loss of nerve fibers that tend to occur within the graft. It is important to direct the individual strands comprising a cable graft in a parallel course, thereby attempting to reduce, so far as one is able to do this, the likelihood of misdirection of axis cylinders from central to peripheral segments of the nerve.

When forming a cable graft it is advisable to glue the nerve strands together at their extremities with plasma, then trimming off a thin slice by means of the special nerve holder and the razor blade described.[14] A flat cut surface is thus obtained and one may proceed to carefully coapt the stumps

of the host nerve to the ends of the graft, utilizing the latex mold in which the plasma clot suture is then carried out. The strands are united with plasma at their ends only so as to allow spreading of the intervening segments in the tissue bed in order that vascularization might more readily develop.

The state of nutrition and the activity of the animal following the use of nerve grafts appeared to have been factors in determining the speed and degree of functional recovery that occurred. In those dogs that had remained in good health and vigorous, the grafts seemed to have shown less reduction in size and the animals appeared to have achieved a greater degree of functional restoration than the animals that were emaciated and relatively inactive. Although this correlation was not invariable, it does seem probable that the greater activity of the more healthy dogs was associated with an improved state of circulation and that vascularization of the nerve grafts was thus promoted. Various nutritional factors as well as the age of the animal probably play a role in governing the result following the use of nerve grafts. The compatibility of tissues of donor and host also must be considered as a possible factor in determining the take of homografts. An attempt was made to test this hypothesis by cross-matching the blood cells and serum of host and donor dogs but, out of more than a score of animals tested, marked red cell agglutination was found in but one pair of animals. Pronounced blood incompatibility between dogs appears, therefore, to be uncommon in non-immunized animals. The graft from this donor dog whose blood was incompatible with that of the recipient did show complete absorption, but absorption of grafts also occurred in animals in which no blood incompatibility was detectable. It is possible that incompatibilities of nerve tissues which are not reflected by blood incompatibility may still be important in relation to the fate of homografts. Even more important is the existence of certain latent incompatibilities which may be shared by blood and tissues and which become manifest only after isoimmunization has occurred.[16] This may explain the instances of skin homografts that seem to take well at first but, after a fortnight or so, undergo dissolution.[11] However, the fact that varying degrees of absorption of autografts is common points to the primacy of some other factor, which in all likelihood is the vascularization of the graft. This must be kept in mind not only during the operation of nerve grafting (and a vascular bed chosen for the graft when this is possible) but also in the period of post-operative care. Massage, heat, exercise and, in short, all measures designed to improve the circulation of the part harboring the graft, and all means of improving the general health of the individual, should be used in an attempt to favor adequate vascularization and take of the graft. Moreover autologous grafts should be used whenever possible in order to reduce the possibility of tissue incompatibility affecting the result. Bunnell and Boyes[3] advocate the use of the sural nerve for grafts since the resultant area of anesthesia is small and seldom annoying. They have been able to obtain as much as a foot of nerve from each calf, thus "allowing ample material

even for a cable graft into a fairly thick nerve." However, there is some evidence that the size of the Schwann tubes within a peripheral nerve stump controls the diameter of the downgrowing nerve fiber.[9] It is thus possible, as expressed by Gutmann and Sanders,[7] "that some of the alleged failures of long autografts in man may be due to the inability of the nerve fibers within small tubes of cutaneous nerve bundles in the graft to enlarge beyond a certain diameter and so conduct impulses with proper time relations to bring about a restoration of the more delicate functions." If this is so then it would appear unwise to use cable grafts made up of cutaneous sensory nerves to bridge gaps in the major mixed nerves in man. On this basis the use of intercostal nerves which contain a great number of motor fibers with large Schwannian tubes would seem preferable. However, it is probable that further light will be thrown on the importance of the size of the Schwannian tube in governing the maturation of a regenerating nerve fiber as a result of studies being carried out in various laboratories and clinics. At present, although the evidence is suggestive, the issue is undecided. Contrary to the findings of Ballance and Duel,[1] Bunnell and Boyes[3] as well as Sanders and Young[13] reported no significant difference in the rate of growth of nerve fibers through fresh and predegenerated autografts.

CONCLUSIONS

1. Very good recovery of sensory and motor function may follow the introduction of fresh homologous cadaver grafts into sciatic nerve defects in dogs. Satisfactory restoration of function has in fact occurred with the use of homografts stored in serum at a temperature of approximately 5°C for 24 to 48 hours. However, complete absorption occurred in 8 of 50 fresh sciatic homografts and in 4 of 50 sciatic autografts. In all thick grafts varying degrees of necrosis and fibrosis appear to be inevitable.

2. Adequate vascularization is a most important factor in determining the take of a nerve graft.

3. Revascularization of nerve grafts develops by the ingrowth of blood vessels from the host stumps and also from the surrounding tissue. Massive necrosis of a graft may occur if blood vessels present in the surrounding tissue are prevented from entering it. There is, then, no justification for the practice of interposing an impermeable membrane between the graft and the surrounding tissue.

4. Although it is imperative that the bed for a nerve graft consist of well-vascularized tissue it has proven futile to attempt to increase the blood supply of nerve grafts by the application of fat-areolar tissue or muscle flaps to them or by tunneling the grafts through muscle.

5. In our small series of experiments on the use of cable homografts compared with single thick homografts the results were only slightly better with the former. Nevertheless cable grafts seem preferable to single grafts for the repair of defects in large nerves since autologous nerves would be available for forming these grafts. On the other hand, if single thick grafts were used

cadaver material would be required. Since necrosis and subsequent fibrotic changes are more apt to occur in homografts than in autografts, the latter should be used whenever possible.

6. When cable grafts are used, its strands should be bound together with plasma only at their ends so that the intervening segments may be separated in the bed of the graft in order that they may more readily acquire an adequate blood supply.

7. The use of plasma clot is essential for suturing cable grafts since considerable damage to the strands accompanies the use of thread suture and, in all, better unions are obtainable with the plasma clot technique.

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RADIOGRAPHIC VISUALIZATION OF AN INTRACEREBRAL DERMOID CYST

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DERMOID and epidermoid tumors of the central nervous system are rare. It is estimated that only about 200 cases have been reported to date. Several publications concerning intracranial dermoids and epidermoids have appeared in recent years so that neurologists, neurosurgeons and neuropathologists have learned to recognize these tumors, especially epidermoids arising in the diploë and causing characteristic x-ray changes in the skull. Weinberger[8] described pneumo-encephalographic findings that he considered typical of intracerebral epidermoids. The case herewith reported is unique in that the lesion was evident in the plain x-ray films before air injection, appearing as a circumscribed area of decreased density within the left frontal lobe.

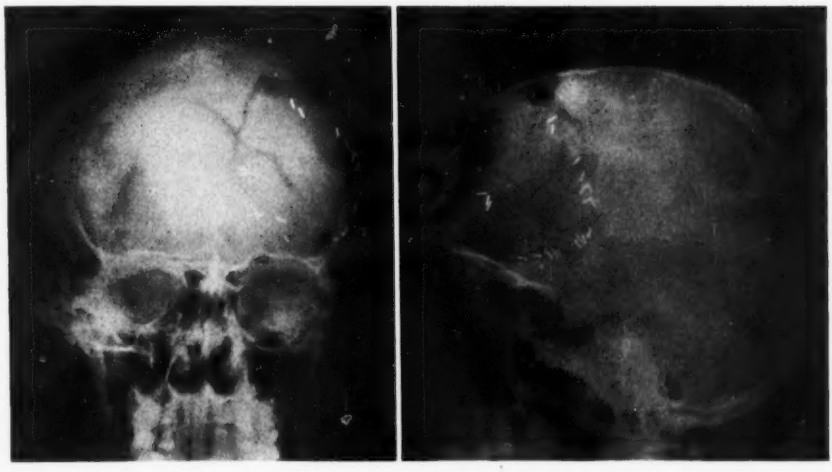
CASE REPORT

R.O., a corporal 20 years old, had been in good health until 7 April 1944 when, while at an overseas base, he had an episode during which he felt peculiar. He was not able to describe

FIGS. 1 and 2. The area of decreased density in the left frontal lobe is indicated by the arrows.

his subjective state more adequately. The next day without warning, while sitting in a chair, he had a generalized seizure lasting 10 minutes. He bit his tongue and was drowsy for several hours thereafter.

The past history discloses a right mastoidectomy at the age of five and a single convulsion



FIGS. 3 and 4. Post-operative x-ray films. The area of decreased density is no longer present.

at the age of eight. His physical and mental development were otherwise entirely normal. He finished high school at the age of 19 and was inducted into the Army at that time. He was returned to the United States on 26 May1944. He complained of daily headaches but otherwise was symptom free.

Examination. The patient was right-handed. Except for a narrowing of the left palpebral fissure (which the patient claimed he always had had) the neurological and general examinations were normal. All laboratory studies, including an electro-encephalogram, were normal. X-rays of the skull showed a large regular ovoid area of decreased density in the left frontal lobe (Figs. 1 and 2).

During the next few weeks the patient's headaches became progressively more severe. A pneumo-encephalogram showed the entire ventricular system to be moderately dilated and shifted to the right. There was a deformity in the anterior portion of the left lateral ventricle.

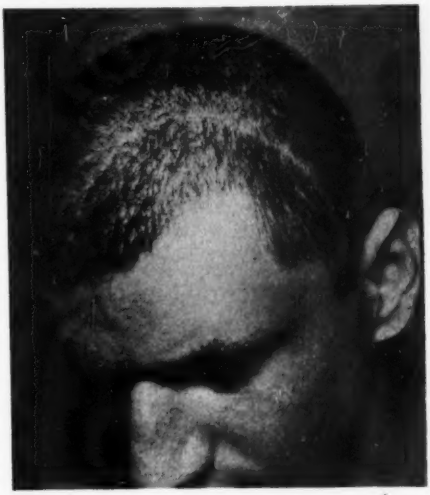


FIG. 5. Patient 2 weeks after operation.

Operation. On 11 July 1944 a left transfrontal craniotomy was done under local anesthesia. A large mass was found in the left frontal lobe about 4 cm. below the surface. It measured about 4×7 cm. and extended mesially to the falx. On opening into the lesion it proved to be a cyst having a wall of paper thinness, ovoid in shape and containing a thin colorless fluid in which many yellowish-white flakes floated. A thick layer of deep yellow material having the consistency of soft paste was adherent to the cyst wall. This material was removed with ease with a blunt spoon. Numerous short blond hairs were mixed in the substance seemingly not connected with any tissue. All in all about 50 cc. of the colorless fluid and about 60 cc. of the semisolid material were removed. As much of the wall as possible was teased out.

Course. Except for an elevation of temperature (100° to 103.4°R) lasting for 10 days, the post-operative course was uneventful. The patient was out of bed on the 11th day. At that time he had no complaints. The neurological status was normal. The patient believed that he had greater ease in his thought processes and he became much more interested in things and happenings than he had been for several months. Mental examination showed no memory or intellectual defect.

EXAMINATION OF THE TUMOR

The material removed at operation consisted of clear fluid in which many yellowish-white flakes floated. No cholesterin crystals were found. In the semisolid deep yellow material many short blond hairs were present. The hairs were free. On microscopic study (Fig. 6) the material seemed lifeless and devoid of living cells except in one section where a small cluster of cuboidal

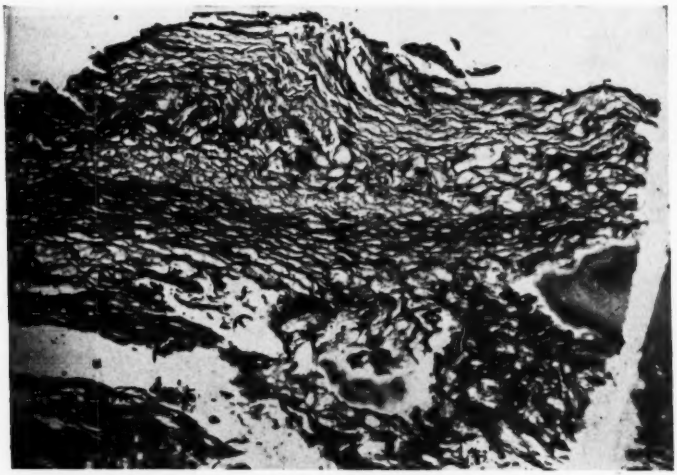


FIG. 6. Photomicrograph of tumor.

cells having deeply staining nuclei was found. The capsule was made up of dense strands of connective-tissue fibers. Below the capsule there was a layer of homogeneous loosely packed material. Beneath this layer there were masses of cells, or rather the outlines of cells, since none of them had nuclei. No blood vessels were seen in any of the sections.

COMMENT

The literature concerning dermoids and epidermoids of the central nervous system has been reviewed by Bailey,[1,2] Rand and Reeves,[7] King,[6] Gross [4,5] and others. Their pathologic characteristics and theories concerning their origin have been thoroughly discussed by Bostroem[3] and Bailey.[1,2] There is still some controversy regarding terminology, but most authors agree that the presence of dermal appendages such as hair warrants the diagnosis of dermoid, while when definite dermal structures are lacking, the term epidermoid should be used. The terms "cholesteatoma" and "pearly tumor" have been used to describe similar lesions. However, both refer to

non-essential characteristics of the tumors so that it seems wise to adhere to the terminology of Bostroem, the epidermoids being the simpler ones, composed exclusively of epidermal cells, whereas in the dermoids, epidermal appendages are also present.

Thus the tumor in this case falls into the category of simple dermoids. Careful study of the material removed failed to reveal any evidence of mesodermal corium, fat, sebaceous glands or other dermal appendages. The appearance corresponds closely to Bailey's description of epidermoid tumors. However, the presence of hair bespeaks for greater activity earlier in the life history of the cyst. Bailey believed that the lifeless appearance of many of these lesions was due to their growing to a certain size and then becoming choked off and lying dormant for years until, for some reason, obstruction of the cerebrospinal fluid pathways occurs and symptoms develop. This theory would explain the chain of events in the present case. At the time of operation the tumor seemed lifeless and was completely avascular. The patient had no focal signs or symptoms at any time. The x-ray appearance in the plain films is the only unique feature of this case. In other respects it is similar to intracerebral dermoids and epidermoids reported previously.

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THE PRECENTRAL MOTOR CORTEX. Edited by Paul C. Bucy. *Urbana, Illinois: The University of Illinois Press*, 1944, 605 pp. (Illinois Monographs in the Medical Sciences, Vol. IV, Nos. 1–4). Price, $4.50 paperbound, $5.50 clothbound.

This comprehensive volume summarizes the important findings on the premotor cortex to the present time and will be met with gratitude by students of neurology. The *Journal* is especially aware of the appreciation of neurosurgeons who have been concerned with abolishing by surgical means the abnormal involuntary movements of the skeletal musculature in patients with choreo-athetosis and tremor. In this excellent survey, planned under the editorship of Dr. Paul C. Bucy, the results of researches are presented by contributors who are preeminent in their particular fields. The book is dedicated to the memory of Otfrid Foerster, who "stimulated the recent renaissance of interest in the activity of the human cerebral cortex, emphasized the correlation of its physiological activity with its microscopic structure" and "insisted on the confirmation of the results of animal experimentation by observations on man." Dr. John F. Fulton in his foreword pays tribute to the late Professor J. G. Dusser de Barenne, whose brilliantly conceived research program led to further developments in the understanding of the precentral region.

The monograph contains eighteen chapters. Gerhardt von Bonin gives a detailed comparative description of the cytoarchitecture of the motor areas in sub-human primates and man. James L. O'Leary analyzes the relation of cytoarchitecture to electrical activity of the cortex. A. Earl Walker describes afferent connections, Paul M. Levin, efferent fibers, Sarah S. Tower, the pyramidal tract, Warren S. McCulloch, cortico-cortical connections, Margaret A. Kennard, somatic and autonomic functions, and Percival Bailey, relationship to the cerebellum. A translation of the excellent but long-neglected paper by Bubnoff and Heidenhain on electrical excitability of the precentral cortex has been prepared by von Bonin and McCulloch. Dr. Bucy observes that this has not been heretofore readily available to all readers and is unfamiliar even to many who work intensively in the field. Wilbur K. Smith's contribution on area 8, the frontal eye fields, was included "since it is concerned with the voluntary innervation of striated musculature, the extraocular muscles, and functions as a suppressor area having many of the same characteristics as area 4s." Theodore C. Erickson's report on the electrical excitability of the human cortex is based on observations from Dr. Penfield's clinic. Paul C. Bucy, in a study of the effects of extirpation in man, reviews the reports of Horsley, Sachs, Foerster and Putnam and gives clinical observations on four cases in his own series. In a following chapter he discusses the relation of the precentral motor cortex to abnormal involuntary movements, and refers to the importance of detailed descriptions in reports of operative procedures and concise definition of the term "premotor cortex," for the better evaluation of future observations. The syndromes of areas 4, 6, 44 and 8, and combined and bilateral lesions are described by Charles D. Aring. A chapter on pathology by Charles Davison includes sixteen case reports and links the clinical findings with the destructive lesions found at autopsy. In the final chapter, on significance of the precentral motor cortex, Marion Hines appraises the results of stimulations and the results of ablations. The monograph includes an extensive bibliography and index.

NEUROCIRUGÍA. PUBLICACIONES Y TRABAJOS CIENTIFICOS. *Santiago (Chile): Instituto Central de Neurocirugía y Neuropatología, Pabellón Harvey Cushing*, 1944: *2*.

This report covers the years 1941 to 1943 and contains original scientific contributions together with collected reprints of papers from the Institute published elsewhere. Director of the Institute is Dr. Alfonso Asenjo, a member of the editorial board of the *Journal*. The

Pabellón Harvey Cushing, in the Hospital del Salvador of the Institute, comprises the departments of neuropathology, neurophysiology, experimental surgery, and the library, the activities of which are described by Dr. Asenjo in his article "El Instituto de Neurocirugía."

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Three papers from abroad have been contributed to this volume: one by Dr. Walter Dandy entitled "Recent advances in the diagnosis and treatment of ruptured intervertebral disks," the second by Professor Herbert Olivecrona on the surgical treatment of Ménière's disease, and the third by Dr. J. Grafton Love on "Tumors of the spinal cord and syphilis: a report of three cases in which syphilis of the nervous system obscured the diagnosis of tumor of the spinal cord."

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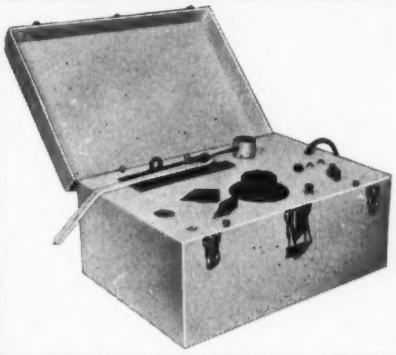

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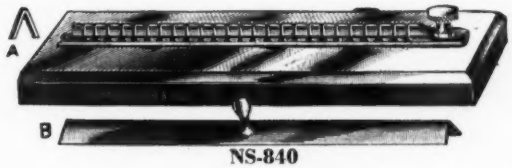

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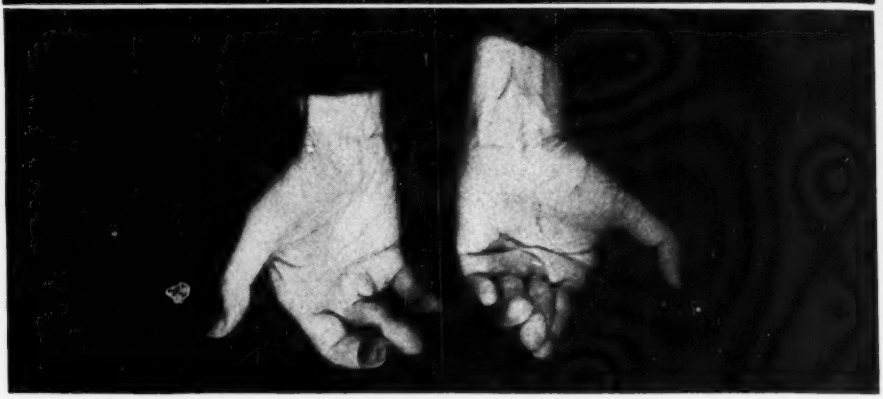

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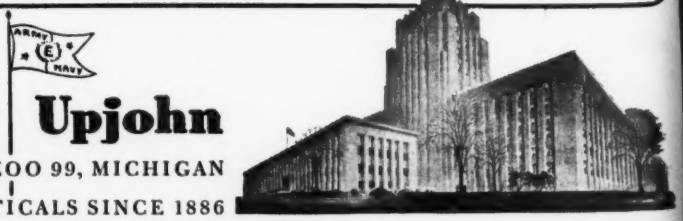

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Neurosurgical Section, Walter Reed General Hospital, Washington, D. C.

(Received for publication October 23, 1944)

IT IS THE PURPOSE of this report to analyze the histologic changes in a number of whole fresh homogenous nerve grafts, placed in peripheral nerve defects in man subsequent to extensive gunshot wounds of the upper and lower extremities. In each of the eight grafts studied, there was no clinical evidence of nerve regeneration after an appropriate time interval had elapsed following transplantation of the neural tissue. When failure of clinical regeneration was manifest, the grafts were exposed under local anesthesia and stimulation studies with a bipolar faradic current were performed. At the termination of the secondary operation, the engrafted segment, including adjacent proximal and distal nerve areas, was excised and was replaced, in seven of the eight cases, with a nerve graft of a different character. The pathologic specimens were fixed in 10 per cent formalin, embedded in paraffin, and stained with Bodian's protargol method for nerve fibers, counterstained in iron hematoxylin and aniline blue.

The problem of nerve grafting is an exceedingly complex one. As in the period 1914 to 1918, the exigencies of war have stimulated renewed investigations into its more academic aspects and into the feasibility of applying any possible advances to the task of nerve grafting in man. With the establishment of the Neurosurgical Section in this hospital, the decision was reached to use homografts for the repair of large nerve defects primarily because the source material was abundant.[9] In addition, there existed certain unassailable experimental studies conducted by Huber and his associates in the period of the last war suggesting that in the experimental animal neuroaxis regeneration was possible through homografts to a degree comparable to that noted in autografts and indeed after simple nerve suture.[6] These studies have been fully confirmed and amplified by our English colleagues in a series of recent publications.[1,3,7]

In spite of these stimulating experimental reports, a survey of the literature devoted to human nerve grafting does not encourage the use of homografts, nor indeed is the reviewer impressed by the number of successful autografts properly evaluated and reported. This is particularly evident in the grafting of large human nerves as compared with small ones such as the facial or digital.

* Col. Spurling is now on overseas duty and this report has been completed in his absence.

Although primary suture of a divided peripheral nerve, accomplished at a much earlier date than previously thought possible, may reduce the number of potential nerve grafts, extensive injuries to the extremities will still consistently afford a group of formidable nerve defects. Furthermore, observations by Highet and Holmes[4] have indicated that extensive resection, mobilization and suture of a peripheral nerve may be followed by failure of regeneration in spite of rigidly guarded postoperative stretching of the involved nerve segment. The validity of such observations has been confirmed among our own cases. Faced by such a technical procedure, a successful

TABLE I

Data on 8 whole fresh homografts used in 7 patients.

Case	Date of		Interval in days	Nerve		Length of graft*	Blood type		Graft removed	Days *in situ*	Graft neurotized†
	injury	graft		injured	graft		rec.	donor			
1.	3/31/43	12/8/43	252	radial	c. peroneal	40 mm.	A	O	6/12/44	187	40 mm.
2.	4/24/43	10/27/43	186	ulnar	median	75 mm.	O	AB	7/18/44	265	18 mm.
	4/24/43	10/27/43	186	median	radial & ulnar	78 mm.	O	AB	7/18/44	265	15 mm.
3.	11/8/42	1/5/44	423	ulnar	?	90 mm.	A	?	7/21/44	198	23 mm.
4.	4/9/43	2/8/44	305	p. tibial	sciatic ½	70 mm.	A	?	7/21/44	164	5 mm.
5.	11/8/42	2/7/44	456	p. tibial	sciatic ½	32 mm.	O	A	6/8/44	122	10 mm.
6.	4/5/43	1/7/44	277	p. tibial	sciatic ½	38 mm.	O	O	6/13/44	158	10 mm.
7.	4/9/43	12/9/43	244	p. tibial	sciatic ½	29 mm.	A	A	6/22/44	196	29 mm.

* Measured after removal and fixation in 10 per cent formol.

† The number of fibers at this point and for several millimeters proximally was in all cases too small to serve any useful purpose.

Note: .003-inch tantalum wire sutures were used in all cases at both proximal and distal anastomoses. Tantalum cuffs were used around the suture lines in all cases but #4 in which fibrin film was placed around both anastomoses, and #3 in which fibrin film was used at the distal suture line and tantalum foil at the proximal.

method of nerve grafting would present the operating surgeon with an attractive alternative.

For these reasons, and because such material is comparatively unusual, it appears desirable to present in some detail this negative contribution to the problem of human nerve grafting. The clinical records of two patients, in whom a total of three homografts was inserted, will suffice to illustrate the salient results of this study.

The clinical histories and gross and microscopic changes noted in a study of the remaining five grafts removed from five other patients differ only in minor and inconsequential detail from those that will be described. They will not be reviewed *in extenso* but the material is summarized in Table I and is available for study at the Army Medical Museum.

CASE REPORTS

Case 5. A.M. (born in 1919) sustained a gunshot wound of the lower third of the right leg on 8 November 1942 with transection of the posterior tibial nerve. On 17 December 1943, the region of the injury was explored and after extensive mobilization of both nerve ends a defect of approximately 32 mm. persisted. The proximal neuroma and distal glioma were joined with a sling suture of .005 tantalum wire in preparation for nerve grafting at a later date. On 7 February 1944, the nerve ends were sectioned at points where distinct nerve bundles could be visualized and the defect filled with a fresh, whole homograft obtained from the sciatic nerve of an adjoining amputation stump revision operation. The donor's blood type was noted later as "A" and the recipient's as "O." The graft was sutured in place with .003 tantalum wire sutures and the anastomosis lines were protected with annealed tantalum foil cuffs. By 8 June 1944, there was no evidence of nerve regeneration and, on that day, the region of the homograft was reinvestigated under local anesthesia. The engrafted segment was embedded in a bed of dense fibrous tissue. When its proximal portion, protected by foil, and its unprotected central segment were being dissected free, the patient complained of pain, suggesting the presence of aberrant nerve fibers. No pain response was noted during dissection of the distal area of the graft.

The proximal nerve end above the upper tantalum cuff was bound down with adhesions, and was edematous but well supplied with blood vessels. These vessels, oriented longitudinally, penetrated the graft for a distance of 10 mm. Beyond this point, a decrease in the number of surface vessels made the graft appear quite white. The epineural surfaces of the nerve ends and the graft, after the tantalum foils had been removed, appeared smooth and glistening. Adhesions about the central portion of the graft had constricted it to a diameter of 7 mm. as compared to one of 11 mm. at the proximal suture line. The distal nerve end appeared yellowish-white and only a few, fine vascular channels were noted in the epineurium. Bipolar faradic stimulation with one volt gave a strong pain response at a point 3 mm. above the proximal anastomosis. Distal to this no response to increasing stimuli was found until the distal nerve end was encountered. Here pain was elicited both upon stimulation and upon transection. The engrafted segment and adjacent neural tissue was resected in one piece.

PATHOLOGICAL REPORT

Gross Examination. The specimen (Fig. 1) is 65 mm. long and 11 mm. in diameter at each end and is hour-glassed to 7 mm. in the midregion where fibrous adhesions have formed a constricting collar completely encircling the nerve. Tantalum wire sutures are present at the proximal junction line of central nerve stump and graft, 15 mm. from the end of the specimen, and also at the distal junction 18 mm. from the other end of the specimen. A few fragments of tantalum foil are seen embedded in the fibrous adhesions near the central third of the specimen. On longitudinal median section the proximal part of the nerve shows ten or more discrete fascicles which become entangled at the suture line. Some of these seem to end at the suture line and others to continue on into the graft. In the central third of the specimen a fatty and fibrous transformation of the graft has taken place and only a few fascicles are seen to have penetrated to the distal third. The constricting fibrous ring around the middle third appears very vascular. The distal suture line is demarcated by the greater abundance of fascicles in the old distal stump and the number and narrow calibre of the strands in the distal end of the homogenous graft. There are fewer fascicles in the distal nerve than in the regenerating central stump and they are separated by narrow fatty areas running longitudinally. The typical glistening white perineural sheaths are present around fascicles in the central and peripheral stump, but not in the graft. In the graft narrow white strands of fibers are present between fat and it will require a silver stain to determine the nature of these. Some of these are also seen in the adhesive collar.

Microscopic Examination. A longitudinal section of the central stump of the nerve to which the graft was sutured shows nerve bundles containing both myelinated and amyelinated nerve fibers spread apart with edema (Fig. 4). Between six large nerve bundles and involving the

epineurium are extensive tracts of dense fibrous and neuromatous tissue. Thick collagenous tissue with a rich blood supply forms a sheath about the regions of the nerve that were adherent to the surrounding tissue. There are a few areas of adipose deposits and large and small mononuclear cells have infiltrated the region diffusely but are also concentrated in a few small foci. In all of the fascicles the orderly arrangement of nerve fibers stops at the junction with the graft and from here distally the fibers become tangled in neuromatous whorls and collagenous tissue (Fig. 11).* The nerve fascicles of the graft have become overgrown with connective tissue and some contain large numbers of fat-laden macrophages (Fig. 5). There are linear and bizarre-shaped deposits of silver impregnated material in some of the tubules, indicating that resorption of the necrotic nerve fibers has not been completed. A few definitely recognizable neuraxes have penetrated for approximately 10 mm. into the graft and then end abruptly amongst macrophages and connective-tissue fibers (Figs. 10, 12). The midregion of the graft shows especially dense scar tissue around the epineurium and between the fascicles (Fig. 5). A considerable amount of adipose tissue is also present. No nerve fibers are seen in the distal part of the graft nor in the distal nerve stump. A dense fibrous sheath surrounds the distal nerve and graft, and at the region of junction so much scar tissue has been thrown across the breach as to make it seem almost impenetrable by nerve fibers (Fig. 6). The old nerve tubules show remaining Schwann cells with fibroblasts and abundant endoneural fibrosis (Figs. 6, 16). Between the fascicles are tracts of dense fibrous tissue and adipose deposits. All of these tissues appear well vascularized.

Case 2. H.B. (born in 1920) received a gunshot wound of the left forearm on 24 April 1943, with extensive loss of soft tissue and with transection of both median and ulnar nerves. Exploratory operation on 20 August 1943, disclosed defects in both nerves that could not be overcome by mobilization and joint posturing. The nerve ends were wrapped in tantalum foil and stabilized by sutures for easier identification at the time of proposed grafting. On 27 October 1943, fresh homografts obtained from amputation stumps were inserted in both defects. The distal and proximal nerve ends were mobilized and the tantalum cuffs removed. The neuromas were resected into normal neural tissue until an orderly grouping of nerve fascicles was apparent. Hemorrhage from the incised nerve ends was controlled with fibrin foam. The graft inserted in the ulnar defect measured approximately 75 mm. and consisted of a whole, fresh homograft. That inserted in the median nerve measured approximately 78 mm. and was formed from two, equal-sized cables. They were held in place by .003 tantalum wire sutures and tantalum wire cuffs were placed around each of the four suture lines.

By 18 July 1944, no evidence of regeneration in either graft could be obtained. On that date, reinvestigation of the grafted areas was carried out. When the foils were removed from the nerve ends and grafts, the epineural surfaces were found smooth and for the most part devoid of adhesions. There were scattered fine, filamentous adhesions about the anastomotic lines. The midportions of both grafts, where no foil had been placed, were constricted by firm bands of fibrous tissue. The proximal stump of the median nerve was bulbous and tapered down to the suture line. This nerve end was pink and well vascularized, and a similar and normal type of vascularization was noted in the proximal 10 mm. of the graft. When the proximal stump and first 10 mm. of the graft were stimulated with a bipolar faradic stimulus of one volt, pain was noted by the patient. Distal to this point, even with increasing stimuli, no painful response could be elicited. The ulnar nerve had expanded but little at its proximal stump and it was also well vascularized. The ulnar graft showed normal vascularization for 10 mm. beneath the foil, but beyond this it was yellowish-white. Stimulation at one volt caused pain in the proximal stump and in the first 20 mm. of the graft. Distal to this point, no reaction was obtained. Since this evidence pointed to regeneration only in the proximal segments of both grafts, and since further regeneration appeared improbable, both grafts and adjacent neural tissues were resected.

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* In this instance, and in others noted, the photomicrograph referred to was prepared from another graft but illustrates a similar condition.

PATHOLOGICAL REPORT

Gross Examination. There are two specimens: (1) A nerve homograft including the distal and proximal stumps of the median nerve to which it had been sutured; (2) a similar specimen from the ulnar nerve (Fig. 2). The median specimen measures 109 mm. in length and proximally has cross sectional dimensions of 11 mm. wide ×6 mm. thick. Involving the proximal stump and the first part of the graft there is a bulbous neuroma, 17 mm. long ×13 mm. wide. A cross section through the proximal part of the nerve reveals at least 15 nerve bundles of varying girths and a rich vascular supply. The epineurium is thickened, the nerve appears edematous and there are small deposits of fat beneath the epineurium. The region (45 mm. long) over which the proximal tantalum sleeve had been placed still shows scattered small fragments of this metal not completely peeled off at operation. Over the proximal site of union a very vascular fibrous tissue is adherent to the nerve, especially posteriorly. Otherwise the surface of the proximal stump and of the two nerves used as grafts appears smooth and glistening. The proximal nerve end, the bulb into which it expands at the juncture with the two grafts, and about 15 mm. length of the graft appear pink and well vascularized. Beyond this for a distance of another 15 mm. the grafts appear white and poorly vascularized. This segment of the graft measures 4 mm. in width and the cross dimension changes but little from here to the distal end of the specimen. The central segment, which had not been protected by foil, is ensheathed with a reddish-gray fibrovascular covering, the two grafts having each been contracted to a diameter of about 1.5 mm. The region of the specimen measuring 25 mm. in length, that had been covered with the distal tantalum sleeve, appears whitish with no adhesions except a few at the distal union site. A cross section of the distal end of the specimen representing the peripheral stump shows approximately ten degenerated nerve bundles which are only recognizable as such by the thin white perineural sheaths encircling them. Otherwise the nerve substance would appear homogeneous and of a yellowish-gray color. Tantalum sutures are seen embedded in the epineurium 13 mm. from the distal end of the specimen. A few bright fragments of tantalum foil, left at the time the distal sleeve was peeled away, are seen at various spots over the distal 25 mm. of the specimen.

The ulnar nerve specimen measures 97 mm. in length, has a diameter of 7 mm. at the proximal end, 4 mm. at the distal end and narrows to a 2-mm. waist about 45 mm. from the proximal end. The proximal 25 mm., including the central stump and the first part of the graft, and the distal 35 mm., including the peripheral stump and the last part of the graft, appear white, smooth and glistening except for a few adhesions immediately over the two suture lines. The middle 37-mm. segment of the graft had not been protected with tantalum foil and is completely sheathed in well vascularized grayish fibrous adhesions. Small pieces of shining tantalum foil are present at various places on the epineurium and tantalum sutures are embedded in the epineurium at the junctions of graft and nerve ends. On cross section the proximal nerve stump shows about ten nerve bundles which are not sharply demarcated. The epineurium appears normal and shows good vascularity and a few storage-fat deposits. Cross section of the distal nerve stump shows yellowish, atrophic nerve bundles encircled by thin white strands of connective tissue.

Microscopic Examination. Median nerve: A cross section through the proximal stump shows 15 medium- and large-calibred nerve bundles and many smaller bundles, some of which contain only a few nerve fibers. In one region these small bundles are aggregated in large numbers, marking the point at which the nerve begins to expand into a neuroma. There is an excess of interfascicular fibrous tissue and the perineural sheaths are abnormally thickened. The epineurium is also thickened and has dense scar tissue on its surface. All parts of this section show a rich vascular supply. Just distal to this point a longitudinal section shows large numbers of small nerve bundles mixed in a conglomerate mass with vascular fibrous tissue. Regions from which tantalum sutures had to be removed before sectioning are marked by thick scar tissue, infiltrating mononuclear cells and a few giant cells. The fascicular arrangement in the proximal stump has given way to a criss-crossing of small nerve bundles mixed with strands of fibrous tissue. The site of union is not sharply demarcated except for a slight

increase in fibrous tissue and the fact that the regenerated nerve bundles show less criss-crossing and run in parallel courses after entering the old fascicles of the grafts. The blood supply within the first part of the graft and the epineural sheath is abundant. Large numbers of amyelinated and slightly myelinated fibers are seen to have penetrated the graft for a distance of 10 mm. and then for the following few mm. they decrease in number while fibrous tissue increases until at about 15 mm. the last of the nerve fibers end in dense scar tissue (Figs. 17, 21, 22). Beyond this point the graft consists of necrotic and fibrosed nerve fascicles buried in dense scar tissue which is quite vascular at the periphery and forms a constricting collar along the segment of graft unprotected by tantalum foil. Some of the old graft fascicles have been heavily infiltrated by macrophages and fibroblasts and are in different stages of fibrosis (Fig. 24). Others show nothing but the degenerated tubules filled with detritus from the breakdown of the nerve fibers and sheaths. The fact that these tubules have not been cleared away may be correlated with their lack of vascularity. It is of interest to note that the fascicles showing the largest number of infiltrating phagocytes have the richest blood supply. The proximal part of the graft into which nerve fibers have penetrated shows a good blood supply to the newly formed nerve bundles. Just beyond the most distal point of nerve fiber penetration, the fibrosed graft appears amply supplied with vessels. A cross section through the distal nerve stump reveals 12 medium sized and 4 small fascicles embedded in heavily fibrosed sheaths. The epineurium and perineurium consist of tissue which is almost tendinous in density and this fibrotic change also involves the endoneurium. Endoneural fibrosis has progressed to such a degree that one sees little more than shrunken Schwann cell nuclei, collagenous tissue and fibroblasts in the distal stump fascicles. In a longitudinal section through the region of the distal anastomosis the degenerated tubules of the graft and the atrophic fibrosed tubules of the distal nerve are seen to be surrounded by dense interfascicular fibrous tissue. The Schwann cell nuclei and cytoplasm appear typically elongated in the distal stump (Fig. 14) and the tubules are so narrowed as to seriously preclude the entrance and maturation of new nerve fibers within them.

Ulnar nerve: A cross section through the proximal nerve stump shows a typical neuromatous proliferation (Fig. 3). Innumerable small nerve bundles enclosed in thin fibrous sheaths are seen throughout the section, even in the epineural region. Connective-tissue septa divide the small nerve bundles into groups of uneven size but only five large circumscribed fascicles are seen. The vascular supply is abundant throughout the section and the tissue appears edematous. A longitudinal section through the proximal nerve stump and graft shows approximately 5 mm. of the neuromatous stump bearing many small criss-crossing and longitudinally orientated small nerve bundles and one large fascicle containing amyelinated and slightly myelinated fibers (Figs. 7, 15). The epineurium appears densely collagenous on one side of the nerve but on the opposite side small nerve bundles occupy the loose areolar tissue immediately within a very narrow rim of a dense epineural fibrous sheath. Several small foci of round cell infiltration and fibrosis, as well as artifactual rents in the tissue are seen in the regions from which the tantalum wire sutures were removed (Fig. 3). At the line of junction between graft and nerve stump the nerve fibers form a bizarre pattern, cross-crossing, reversing their course and becoming generally entangled in the scar tissue of the breach (Fig. 3). Many of these fibers are seen to have penetrated the graft fascicles (Fig. 8) and here they are orientated normally and are guided distally by the old neurolemmal sheaths for a distance of at least 18 mm. (Figs. 18, 23). At this point in the sections studied the neuraxes end in the graft tubules. Capillaries, macrophages and fibroblasts seem to have penetrated for the same distance into some of the old fascicles as the nerve fibers with their Schwann cells (Fig. 9). Some graft fascicles merely show autolysis with no infiltration of macrophages or organization by fibroblasts, whereas others contain large numbers of fat-containing macrophages and fibroblasts and dense collagenous deposits (Fig. 13). Just distal to the suture line a narrow collar of dense fibrous adhesions constricts the graft. A tantalum ligature had been placed around the tantalum sleeve at this point. For the most part the short length of proximal graft that had been wrapped in foil shows a thin epineural sheath devoid of adhesions, but immediately beyond this the graft is densely fibrosed and surrounded by a very vascular collagenous sheath.

Throughout the remainder of the graft, fascicles are seen in various stages of autolysis, resorption and fibrous organization. Blood vessels and large numbers of phagocytes appear to have had no difficulty in penetrating some of the bundles of degenerated nerve tubules. Whereas in other instances the old Schwann cells have become necrotic and the degenerated sheath and fiber remains have not been resorbed. The histopathologic changes seen in the distal stump of this nerve are essentially the same as those described for the median nerve. A cross section reveals a remarkable example of advanced fibrosis. Ten atrophic nerve fascicles are enclosed in scar tissue which is densely fibrillar and relatively poor in fibroblasts. This scar tissue, beginning at the surface of the nerve, encircles and lies between the remaining fascicles which show extreme endoneural fibrosis, and a fibrosed perineurium fused with the interfascicular scar tissue. Some of the old fascicles have been completely replaced by scar tissue while others show crescentic or semi-circular areas of complete fibrosis with the remainder of the fascicle consisting of narrowed neurolemmal tubules, atrophic Schwann cells and fibroblasts enmeshed in fibrotic processes of a slightly earlier stage. The vascular supply of the distal stump appears to be abundant (Fig. 14) although some of the vessels are sclerotic.

DISCUSSION

In order to complete the clinical record of these patients, the statement may be made again that all eight whole, fresh homogenous grafts, inserted by four different operators using almost identical operative techniques, were abject clinical failures. On the other hand, it was quite possible to demonstrate the growth of neuraxes into the proximal portion of the graft for varying distances in each individual case, a growth, however, that failed to mature under the influence of several adverse factors. In two, nerve fibers were indeed demonstrated in the distal portion of the graft (Figs. 19, 20). The basic factors of growth implied in the terms autograft, homograft and heterograft are not known but their effects may be visualized in tissue stains. These tissue changes and the more obvious changes relating to technical procedures and mechanical hazards may be discussed under the following headings.

1. *Time Interval Between Injury and Operation.* The shortest interval was 186 days in Case 2 and the longest 456 days in Case 5. Surgeons emphasized in the last war and are again stressing the importance of early definitive intervention in nerve injuries. Any rule of action applying to simple anastomosis may not necessarily apply to nerve grafting but in none of these cases could the time interval be considered short. The main adverse factor to be obviated by early grafting is fibrosis of the distal stump, warned against by Borchardt[2] in 1915 and studied in detail recently by Holmes and Young.[5] Although this condition was present to a marked degree in all nerves, it may be dismissed as important but academic here since only a few fibers in two cases achieved this penultimate goal. Multiple-stage operations, necessary in this pioneering effort because of the lack of more refined grafting facilities, can only compromise the success of nerve grafting. The time period after injury is prolonged and the increased scarring of the graft bed, distortion and possible stretching of the nerve ends and chance of secondary infection are not conducive to technical perfection. We are convinced from these and subsequent experiences that definitive surgery of

peripheral nerve injuries should encompass the possibility of early nerve grafting.

2. *The Condition of the Wound.* This factor should be considered in sequence since the time interval between injury and repair may influence the immediate environment of the graft, that is, the graft bed. Potential infection should be of little concern with the recent advances in bactericidal substances. Wound infection followed in Cases 5 and 6, originally infected at the time of injury, and must always be considered a hazard when tissue, such as a graft, is inserted into an operative wound. In subsequent grafts, pre- and postoperative penicillin therapy has been instituted. In all cases, the graft bed consisted of firm, indurated scar tissue which could not be readily revised. The inflicting force responsible for major nerve defects is reflected in widespread fibrosis in soft tissue and muscle. The adverse influence of such a graft bed is further discussed under heading 5.

3. *The Condition of the Nerve Stumps Prior to Grafting.* As a necessary prelude to grafting, the proximal neuroma and distal glioma had been resected through what had appeared to be normal-appearing fascicles. This point has been briefly noted under heading 1. That such supposedly normal fascicles may contain far too much connective tissue has been commented upon by Seddon, Young, and Holmes[8] and the need for a rapid histologic method for an immediate survey of the condition of nerve stumps is apparent. Histologic study of the proximal stumps removed with the graft segments indicates that in most cases neuromata had persisted or new ones developed. This factor is not advanced as an explanation for the lack of fibers in the graft since the overproduced neuromatous stumps are notoriously rich in these elements. It is intended merely to emphasize the point that if a gap exists that necessitates a graft, the proximal and distal nerve ends must be prepared through normal-appearing tissue. This basic principle applies equally well to the scarred, often edematous nerve trunk that may lie just central to the neuroma. The distal nerve end may be extensively fibrosed in long-standing injuries and in such instances it is doubtful whether any degree of distally placed resection will attain neurolemmal tubules adequate for the reception and maturation of nerve fibers.

4. *The Postoperative Course.* This was uneventful except in Cases 5 and 6, where the wounds suppurated. Judging by the appearances of the grafts at the time of removal, they had not been involved in the infection. Roentgenological study of the tibia in Case 7 revealed an osteomyelitic focus and there had been an infection in the region of the graft bed one month before its insertion. Again, the graft did not appear adversely affected by this contiguous infection. Up to this point, the factors influencing the survival of the grafts were little different from those operating for and against the fate of simple nerve anastomoses. The following points are more applicable to the present problem.

5. *The Operative Technique.* This was essentially similar in Cases 1, 2, 5, 6 and 7, and has been described in detail by one of us in a recent publication.[9] Tantalum wire, .003 inches in diameter, was used as an interrupted

suture and every effort was made to keep it within the epineurium. Gross and microscopic studies of some grafts showed that the sutures were actually intraneural and sometimes stay sutures were deliberately placed there. Very little reaction occurred about the wires but it was evident at the proximal breach, one region where it is difficult to exclude fibroblasts by any technique. Here small masses of round cells, giant cells and fibrous tissue marked the tissue-traumatizing effect of these intraneural sutures.

The wrapping of nerve sutures in foil represents the continuation of a procedure initiated 70 years ago with the first graft experiments and, as may be seen from our results, still needs improvement. However, the findings noted in connection with the application of tantalum foil cuffs in these cases appear highly significant. As has been repeatedly stated in the protocols, the nerve ends and segments of grafts protected by the foils were relatively normal in appearance where the unprotected segments were ensheathed by constricting adhesions. Since in every case listed it has been possible to demonstrate the growth of neuraxes into the graft but only to the slightest degree in two cases beyond these constricting areas, this point will deserve close and further scrutiny. In Case 3, where foil was placed around the proximal junction and a protein film about the distal anastomosis, the beneficial effect of the former is well illustrated. These findings, repeatedly verified, suggest that the entire graft may need mechanical protection from the adverse influence of the graft bed tissues. This supposition will be considered further in a discussion of the vascular supply of engrafted segments.

6. *The Source of the Graft.* The homograft in each instance was secured from a case of limb reamputation proceeding simultaneously with the graft operation. It is important to stress the fact that these were reamputations or revisions of stumps and to recall that nerves from such cases are always fibrotic and degenerated within a few centimeters of the neuromatous stump. The grafts were inspected for gross pathologic changes but specimens were not taken for histologic check on the possible existence of endoneural fibrosis.

The grafts were inserted as whole nerve segments. A study of large nerve trunks will reveal a considerable quantity of useless, nonviable tissue obviously detrimental to successful penetration of neuraxes into the proper tubules of the graft. The dense fibrotic changes illustrated in these grafts may be attributed in part to the existence of viable fibroblasts in the grafts. One of the main points of difference between successful animal homografts and human failures may lie in the girth of the engrafted tissue. Two or three millimeters is considered a large enough diameter in rabbit nerve grafting and the posterior tibial nerve of this animal has scarcely more extraneous tissue than a single fascicle dissected from a human sciatic nerve. Blood vessels, fat, epineurium and a considerable amount of interfascicular tissue may be removed from the actual neural tissue of a large human nerve trunk. The remaining fascicles may be split longitudinally into ideally sized cable grafts. In Case 2, two cable grafts were inserted in the median nerve defect and although their combined cross section was less than that of the proximal

stump, they received nerve fibers in large numbers. These remained viable in the two-centimeter-long section of graft protected by foil.

7. *The Influence of Blood Groups.* No attention was paid to the blood groups of the donors or recipients. Time permitting, compatibility between host and donor's blood groups might be ascertained prior to grafting. A peripheral nerve is a complex structure made up of many cell types and cell products, most of which bear isoagglutinogens. Until more is learned about the nature of the reaction between these and the host agglutins, it would seem better to check compatibility in those cases in which autografting is not feasible. Where possible the blood types of all donors in this series were ascertained and these, with the recipients' blood types, are listed in Table I. It will be noted that Case 7 (type A), receiving a graft from within the same blood group, fared no better than Case 5 where, for instance, an A donor contributed to an O recipient. The probable influence of this factor remains an unsolved problem.

8. *The Vascular Supply of the Homografts.* No quantitative method was available for evaluating the degree to which the nerve stumps and different graft zones were vascularized. Nor could any estimate be placed upon the functional capacity of the observed vascular channels. However, the presence of blood vessels in all tissues studied has been recorded in the histologic reports and may be briefly summarized here. In all of the proximal stumps and grafts studied, areas exhibiting good nerve growth were always well vascularized, even in the presence of the fibrous network typical of a neuroma. Although vessels were present in some regions throughout the entire lengths of all grafts, nerve fibers had penetrated only one to two centimeters. In the zones entered by neuraxes, capillaries were well oriented along the route of the old tubules, and many old fascicles, even in the proximal graft, were found to have been invaded by vessels, macrophages and fibroblasts and not by nerve fibers. Some of the old graft fascicles beneath the tantalum cuffs were supplied by vessels growing longitudinally from the proximal stump, while others received their blood supply from the surrounding richly vascularized adhesions. Progressing distally into the graft, the vascularity decreased as the fibrosis increased and thus the same physical block might be said to have inhibited the sprouting of endothelium and nerve fibers. Possibly time favored intrinsic as well as extrinsic fibrotic processes in the graft since the penetration of the first centimeter of the graft by neuraxes seems to have been accomplished before an overwhelming fibrous growth had taken place. In the time intervening before the more distant regions of the graft could be reached, opportunity was provided for establishing a degree of fibrosis capable of blocking nerve fibers and diminishing vascularization.

Old graft fascicles not entered by vessels remained unresorbed and they were not always internally fibrosed. Immediately adjoining such fascicles it was not unusual to find others penetrated by blood vessels even though they appeared to be surrounded by equally dense collagenous tissue. The diffi-

culty encountered in attempting to correlate neurotization of the grafts with vascularization will be appreciated upon examining the following five coexisting conditions observed in the graft fascicles near the proximal anastomotic line: (1) Entered by vessels, macrophages, fibroblasts, connective-tissue fibers, neuraxes and Schwann cells; (2) entered by vessels, many macrophages and relatively few fibroblasts and connective-tissue fibers; (3) entered by relatively few macrophages and many fibroblasts and connective-tissue fibers; (4) completely collagenized and (5) not entered by any cells or fibers. It would seem safe to conclude that a rich blood supply to the tubules within a graft fascicle did not guarantee their neuromotization, but that intra- and interfascicular fibrosis unquestionably defeated it.

SUMMARY

Failure of clinical regeneration and the gross and microscopic changes accompanying such clinical failure have been reported and discussed in eight instances of the grafting of whole, fresh homogenous nerves in man. It is apparent that the nerve fibers of the host nerve can penetrate such engrafted segments in appreciable numbers. From an evaluation of the dense fibrotic reaction that concomitantly invades such grafts, it is clear that maturation of such nerve fibers is improbable. Although whole fresh homografts furnish an easily accessible source for human nerve grafting, their further clinical use must be decried. A study of such grafts has disclosed several factors, in addition to tissue incompatibility, that may influence to a considerable degree the success or failure of any type of nerve grafting. These factors have been discussed in detail in the body of the report. The stimulus behind nerve fiber regeneration is a potent one. The actual bridging of the gap between regenerating fibers and the distal nerve may be realistically achieved by the summation of a multitude of laboriously achieved technical and biological refinements. It will not be achieved by the use of any all-encompassing method of grafting such as is implied by the words "homograft" or "autograft."

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PLATES

All of the tissues were fixed immediately in 10 per cent formalin and sectioned in paraffin at the Pathology Laboratory of the Walter Reed General Hospital. The sections were impregnated by the Bodian silver method and counterstained with hematoxylin and aniline blue by Sergeant G. J. Keller of the Army Institute of Pathology. The photomicrographs were prepared by Mr. Roy M. Reeve of the Army Medical Museum and the photographs by the Photographic Laboratory of the Army Medical School. The photomicrographs have been placed with their proximal ends to the right.

PLATE I

FIG. 1. *Case 5.* Whole fresh nerve homograft (½ sciatic) sutured into posterior tibial nerve defect 7 February 1944 and removed 8 June 1944. Tantalum sutures (.003 inch) were used at both junctions and .00025-inch tantalum foil was wrapped around the suture zones but not around the midregion of the graft. Dense adhesions are shown in the form of a constricting collar around the unprotected part of the graft. The distal stump extends from 7 to 27 mm. on the scale, the graft from 27 to 59 mm. and the proximal stump from 59 to 72 mm. Nerve fibers had grown 10 mm. into the graft.

FIG. 2. *Case 2.* Median nerve whole fresh homograft inserted into an ulnar nerve defect on 27 October 1943 and removed on 18 July 1944. Details same as in Case 5. Graft extends from approximately 15 to 90 mm. on scale. Adhesions are seen around the proximal suture line and the dark midregion which had not been surrounded by foil. Nerve fibers had grown 18 mm. into this graft.

FIG. 3. *Case 6.* Longitudinal median section through the proximal union. At the right the proximal stump is shown to be neuromatous and this condition extends into the first part of the graft. Nerve fibers were present in the dark fascicles of the graft at the left but were embedded in endoneural fibrotic processes, surrounded by dense fibrous tracts and enclosed within a thickened epineurium.

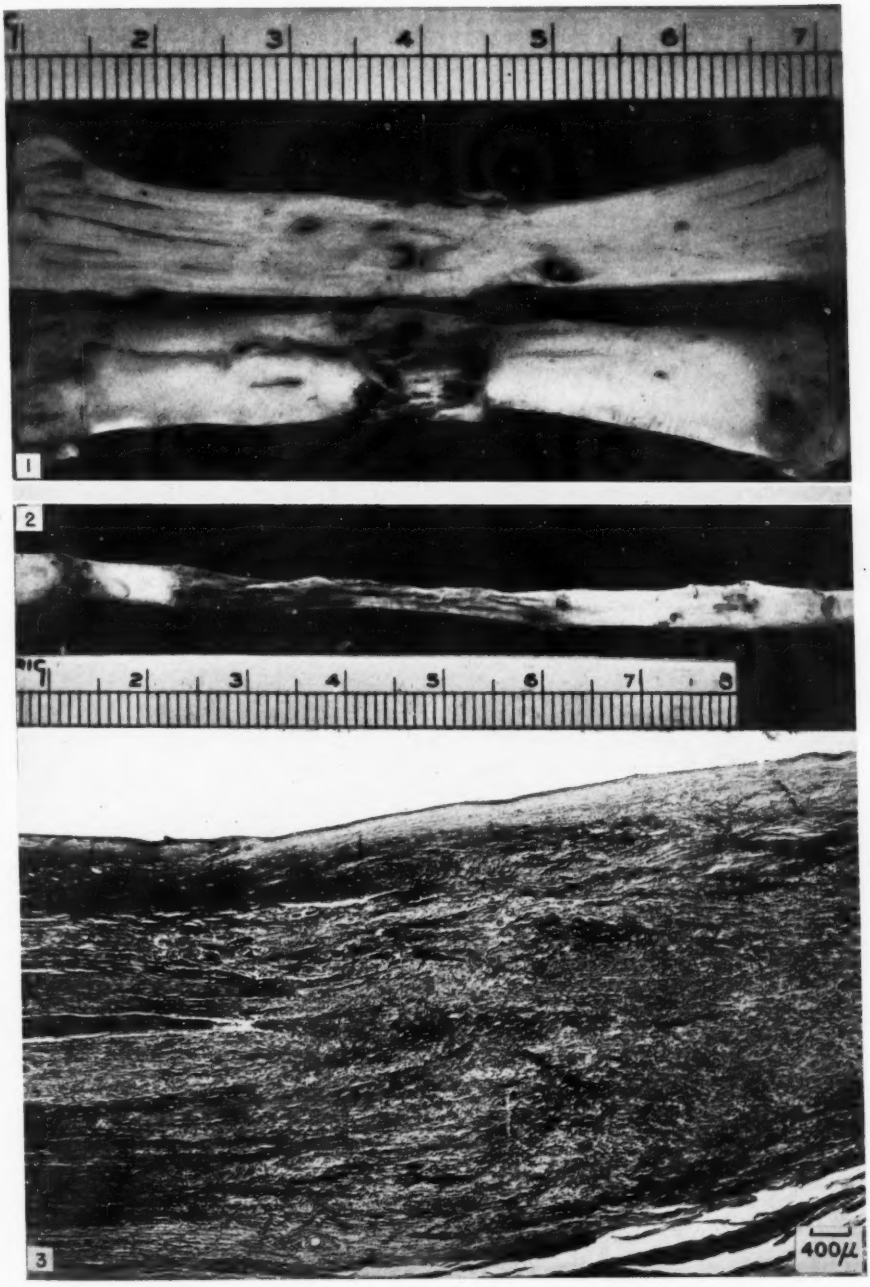

PLATE I

PLATE II

FIG. 4. *Case 5.* Junction zone showing edematous fascicles and interfascicular fibrosis in the proximal stump at the right, neuromatous criss-crossing of regenerated nerve fibers, considerable suture-line fibrosis, and axis cylinders penetrating the graft.

FIG. 5. *Case 5.* Proximal graft at the right shows fibrosed fascicles in which higher magnification studies demonstrated a few nerve fibers. Midregion of the graft at the left shows degenerated fascicles with dense fibrous tracts between them.

FIG. 6. *Case 5.* Junction zone showing fibrous barrier at right between graft and the distal stump closing off the distal nerve fascicles. These fascicles consist of Schwann cells and tubules and show endoneural fibrosis. There is considerable fatty and collagenous tissue between fascicles.

PLATE II

PLATE III

FIG. 7. *Case 7.* Longitudinal median section through the proximal stump at the suture line. Fibroblasts have penetrated this nerve bundle along with Schwann cells and regenerating axis cylinders, and excess fibrous tissue has been formed.

FIG. 8. *Case 2.* Longitudinal median section through the proximal part of the ulnar graft 8 mm. from the proximal suture line, showing large fibroblasts with ovoid nuclei amongst collagenous bundles, Schwann cells with dark, elongated nuclei and fine axis cylinders. Some of the axis cylinders entangled in connective tissue appeared granular and lightly impregnated.

FIG. 9. *Case 2.* Region approximately 5 mm. distal to that shown in Fig. 8. In the upper left corner may be seen large fat-laden macrophages with the growth tip of an amyelinated fiber reaching around their upper borders. Capillaries had penetrated slightly more distally in this fascicle which still contained unresorbed nerve fibers and sheath remains.

FIG. 10. *Case 7.* Longitudinal median section through the graft 10 mm. distal to the proximal suture line, illustrating the contracture of infiltrating collagenous tissues upon the nerve fibers and, at the extreme left, fibrous tissue thrown across the old tubular pathways. Several "defatted" macrophages are seen amongst the collagen bundles and axis cylinders.

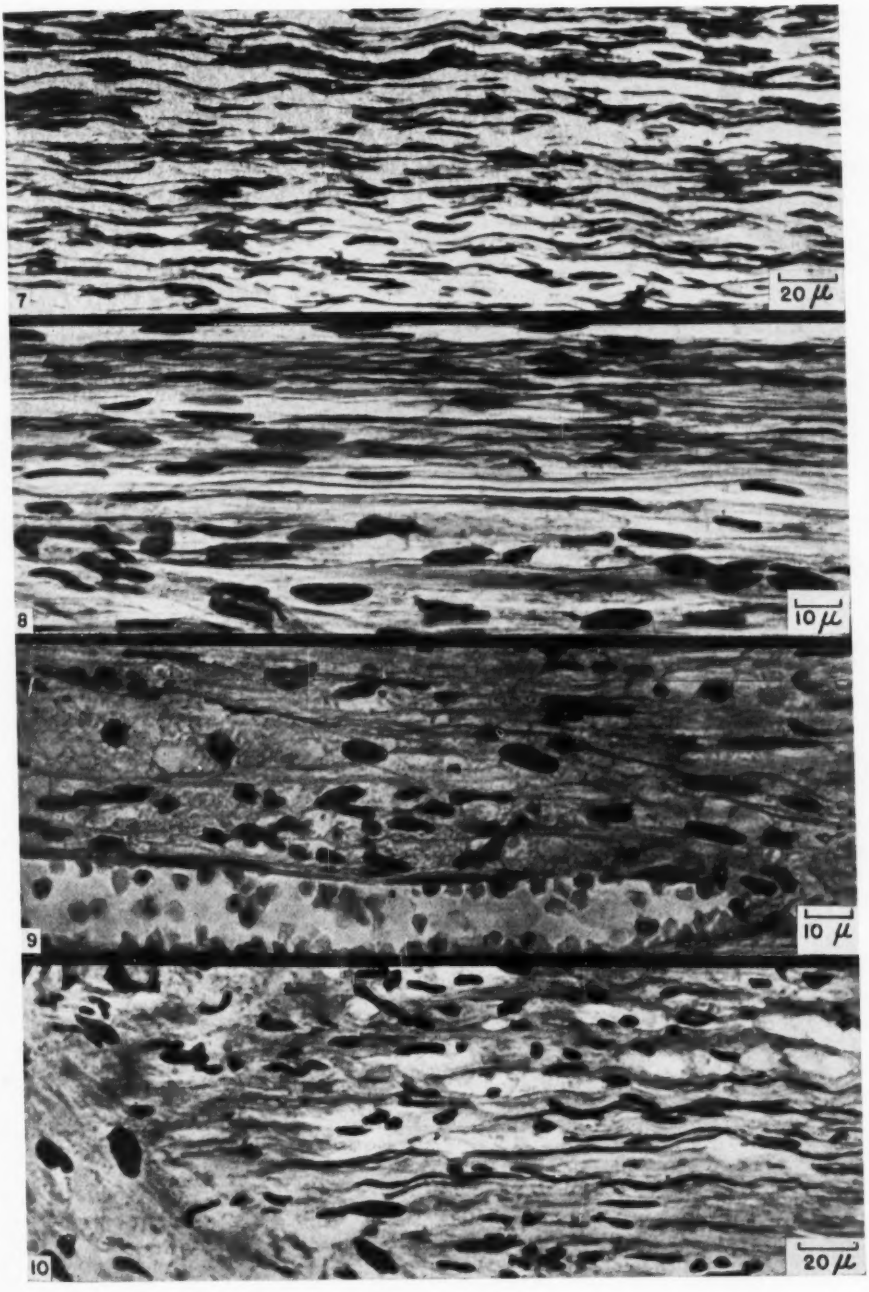

PLATE III

PLATE IV

FIG. 11. *Case 1.* Intrafascicular fibrosis and criss-crossing of small nerve bundles entangled in connective tissue invading a proximal stump fascicle near the suture line.

FIG. 12. *Case 1.* A few amyelinated fibers are present amongst macrophages and collagenous bundles in a degenerated graft fascicle approximately 25 mm. distal to the proximal suture line.

FIG. 13. *Case 7.* Macrophages and collagenous bundles in a degenerated fascicle in the distal part of the graft.

FIG. 14. *Case 5.* Longitudinal, median section through a distal stump fascicle (see Fig. 6) showing shrunken neurolemmal tubules and a blood vessel. No nerve fibers are seen.

FIG. 15. *Case 7.* Cross section through an edematous, neuromatous nerve bundle just central to the proximal suture line. The axis cylinders in the multiple small nerve groups have become surrounded by a fine endoneural mesh and only a few have acquired a normal-appearing myelin sheath.

FIG. 16. *Case 2.* Median nerve. Cross section of distal stump fascicle showing empty Schwann tubules, fibroblasts, and blood vessels. This is largely an endoneural fibrous network and although nerve fibers might readily penetrate it there would be but little room for their expansion and maturation.

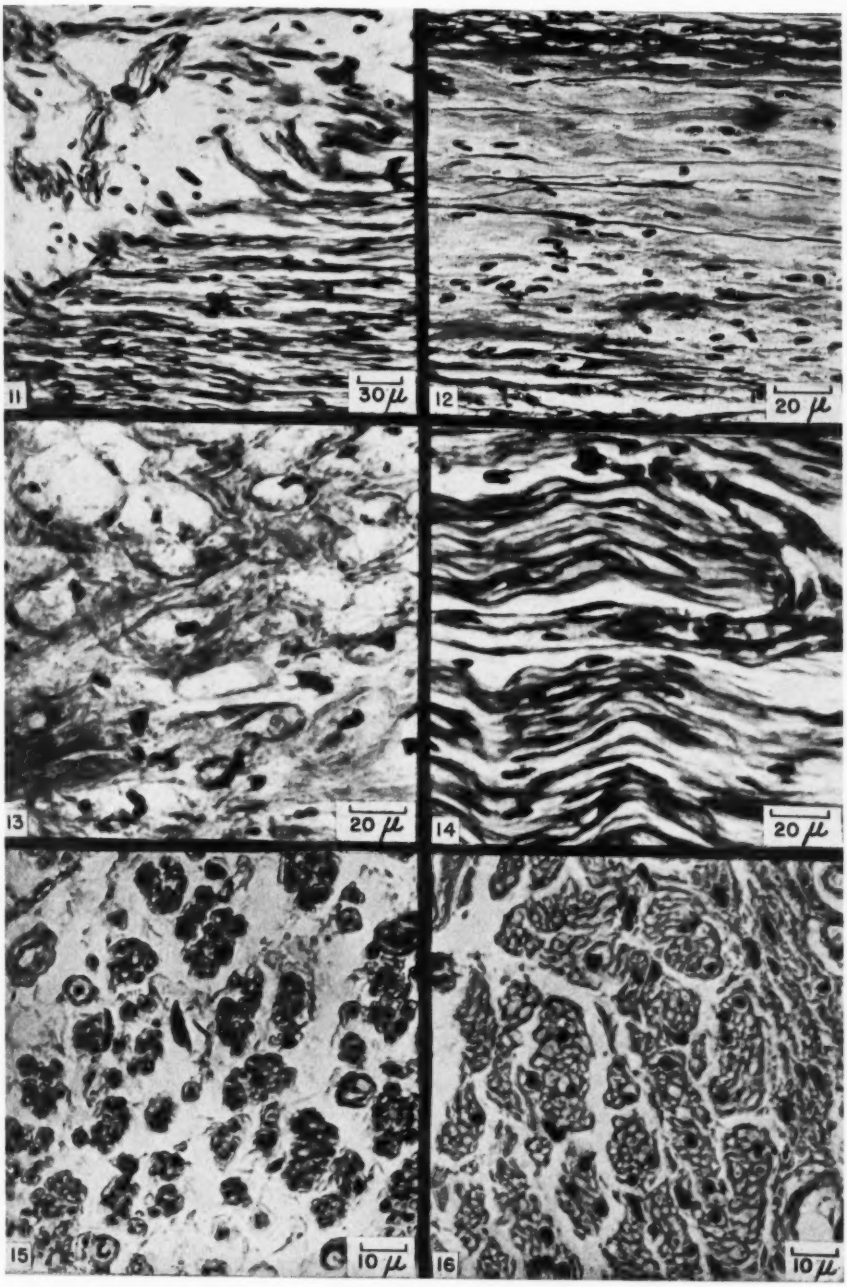

PLATE IV

PLATE V

FIG. 17. *Case 2.* Oil immersion study of one of the atrophic, fibrotic graft fascicles shown in Fig. 22. Thick fibrous septa are seen between the small fibrosed nerve bundles. The edema present at the time of fixation accounts for the shrinkage observed.

FIG. 18. *Case 2.* Ulnar nerve. Oil immersion study of the dark area of the larger, neurotized fascicle shown in Fig. 23. Macrophages and blood vessels are present and some of the fine axis cylinders appear to have grown along the inner and outer surfaces of the old neurolemmal tubules, while others are enmeshed in a fibrous network.

FIG. 19. *Case 7.* Longitudinal section through a distal stump fascicle showing Schwann cells and one well impregnated axis cylinder. Others that appear lightly impregnated and granular may represent degenerating fibers. The Schwann cytoplasm and neurolemmal sheaths are not darkly stained.

FIG. 20. *Case 1.* Essentially similar to Fig. 19, with the Schwann cytoplasm and connective-tissue fibers more in evidence.

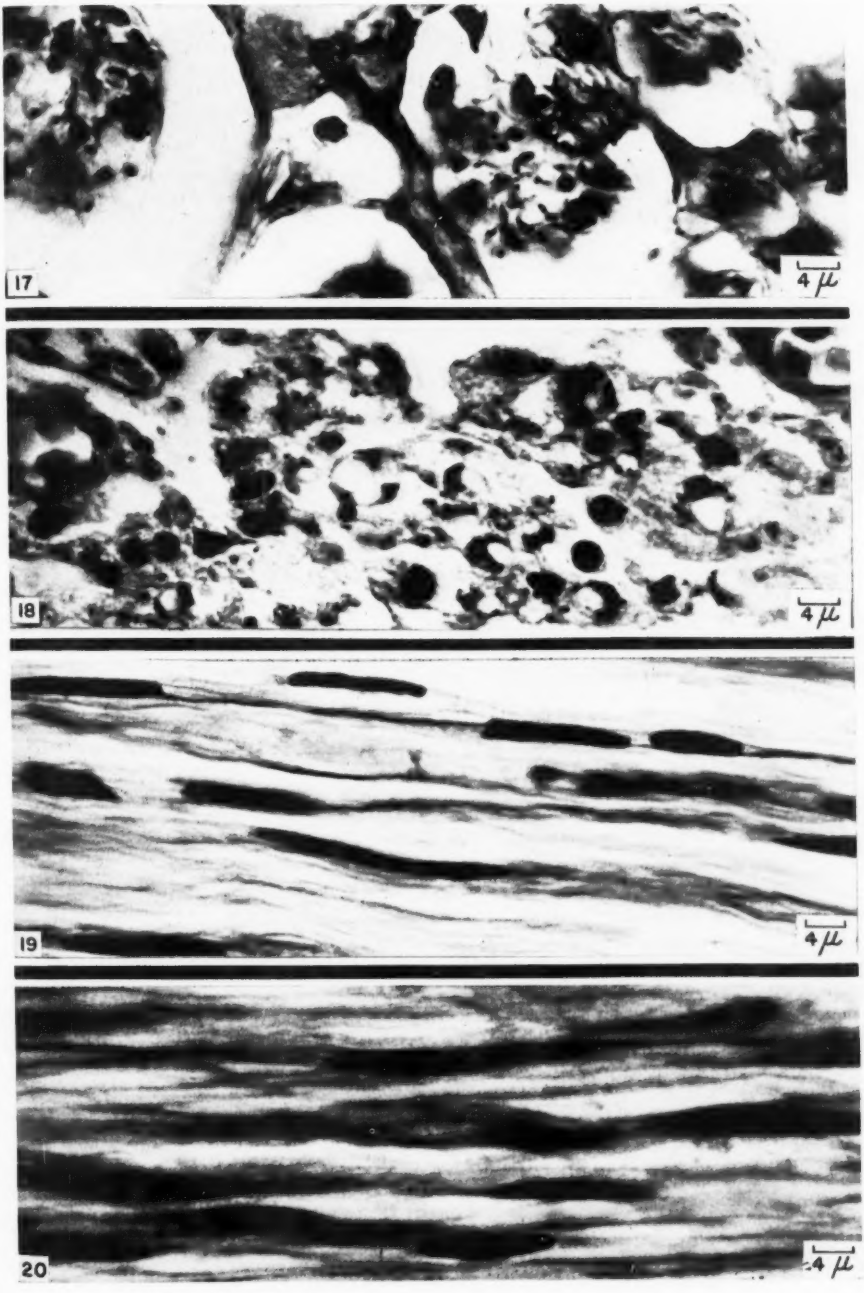

PLATE V

PLATE VI

FIG. 21. *Case 1.* Cross section through region of graft 14 mm. distal to the proximal suture line. The atrophic graft fascicles contain amyelinated and slightly myelinated nerve fibers amongst endoneural fibrous tissue. Throughout the section may be seen multiple small nerve bundles in a richly vascularized fibrous bed typical of a hard fibrous neuroma.

FIG. 22. *Case 2.* Median nerve 15 mm. distal to proximal suture line. Essentially similar in all details to Fig. 21. A large neuromatous bulb was present proximally in this case.

FIG. 23. *Case 2.* Ulnar nerve. Cross section through the graft 18 mm. distal to the proximal suture line. Most of the fascicles show unresorbed nerve detritus and little or no blood supply within. The dark areas of the two fascicles on the left represent regenerated axis cylinders. The epineurium is thickened. The interfascicular regions are densely fibrous but richly vascularized.

FIG. 24. *Case 2.* Median nerve. Cross section through the graft 31 mm. distal to the proximal suture line, showing different degrees of fibrosis of the old graft fascicles. The upper left half of the section shows the dense scar tissue and adhesions that bound the graft to a fibrous bed.

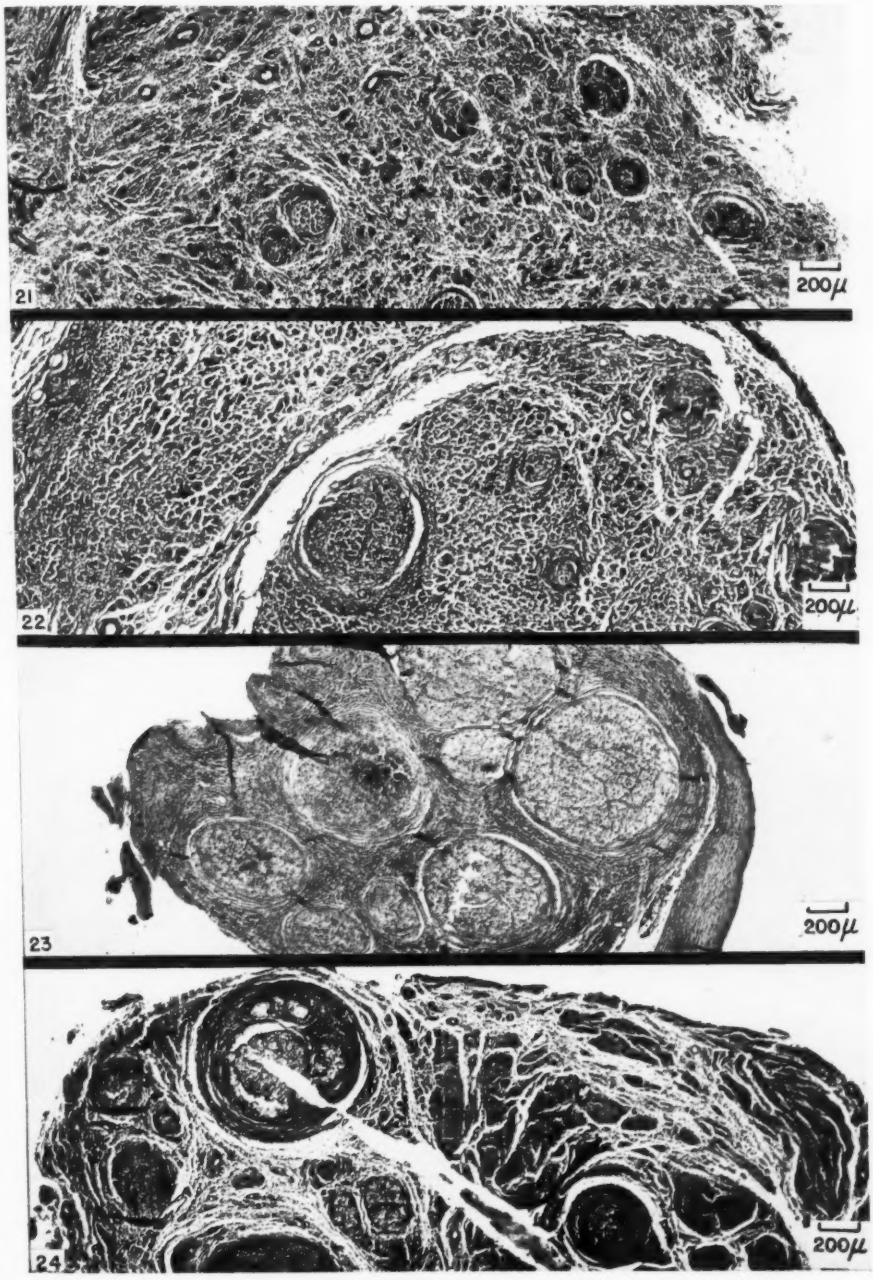

PLATE VI

THE COMBINED USE OF FIBRIN FILM AND CLOT IN END-TO-END UNION OF NERVES

AN EXPERIMENTAL STUDY*

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IN THE past few years attention has been focussed again on the study of peripheral nerve repair. The conventional "thread" method of end-to-end union of nerve stumps has been re-examined, and improvements or substitutions advanced.[4,13,14,15,16,17,18,20,21,23] The fibrin-adhesive technique here reported offers technical advantages which may prove of value for nerve repair as well as for other uses. However, further work on the preparation and standardization of a fibrin film that gives minimum tissue reaction, and additional experimental studies, duplicating as closely as possible in animals the conditions encountered in the human, are required before the technique can be recommended as a substitute or supplement for prevailing clinical methods.

The fibrin-adhesive method involves the application to the apposed nerve stumps of a thin sheet of fibrin surfaced with a layer of clotting fibrinogen which binds the film to the epineurium of the nerve. The fibrin film serves both to maintain apposition of the cut ends and to form an envelope around the nerve wound. The film and clot are in contact only with the outer surface of the nerve and thus should create no obstacle to nerve repair; no foreign material is introduced into the nerve substance itself or between the cut surfaces. In these respects the technique is similar to the tubular splicing method of Weiss.[18,20]

In the course of analysis of the fibrin-adhesive union, *in vitro* and *in vivo* studies were made of the mechanical factors influencing the tensile strength of the nerve splice, of the postoperative changes in tensile strength due to healing, and of the speed with which regenerating nerve fibers bridge the wound region. These studies, in addition to histological observations of the nerve repair and of the tissue responses to the presence of the film, are included in the present report.

THE FIBRIN-ADHESIVE METHOD

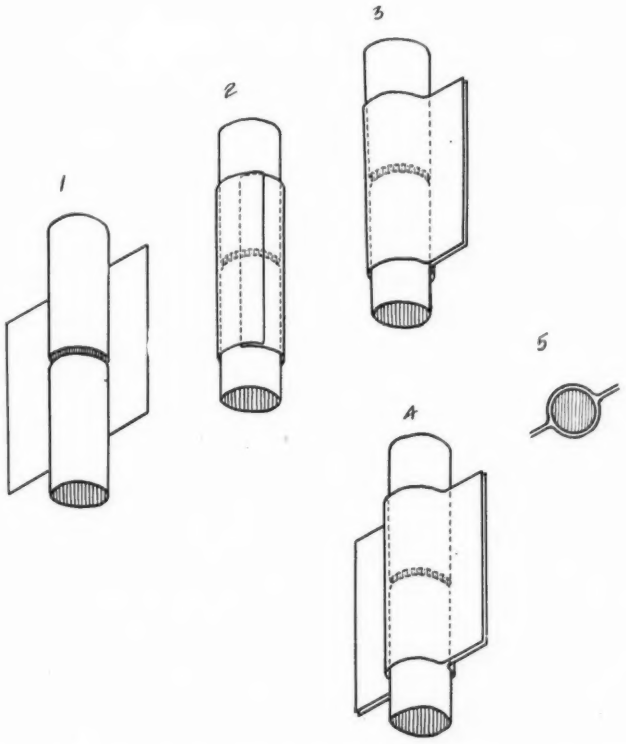
From the results of experiments which are detailed below, the fibrin-adhesive method of end-to-end union of nerve stumps has been elaborated. In the most satisfactory form thus far developed, the method consists of the following steps:

* The products of plasma fractionation employed in this work were developed from blood, collected by the American Red Cross, by the Department of Physical Chemistry, Harvard Medical School, Boston, Massachusetts, under contract recommended by the Committee on Medical Research, between the Office of Scientific Research and Development and Harvard University.

1. Type P. human fibrin film (for properties of film, see below) containing 3 mg. of fibrin per sq. cm. is soaked in sterile saline solution for 2–3 minutes.

2. The saline solution is then pressed from the film between gauze sponges and the film immersed for 2–3 minutes in a sterile thrombin solution containing 1–2 units of thrombin per cc.

3. The strip of film is then drained and permitted to dry on a flat surface until its edges



FIGS. 1–5. Diagrams showing methods of application of adhesive to nerve stumps.
FIGS. 2, 3. Alternative methods of enveloping the stumps with a single leaf of film.
FIG. 4. The two-leaf method (in cross section, Fig. 5).

begin to curl. It may be necessary in order to obtain uniform drying to wipe some parts of the film free from excess thrombin solution.

4. One side of the film is surfaced with a thin layer of 2 per cent fibrinogen by running it successively over the surface of the solution and out over the edge of the fibrinogen container. The second part of this maneuver removes the excess of solution and leaves a thin glistening layer of fibrinogen on one side of the film.

5. The film is then introduced into the wound area and the nerve stumps are apposed over its fibrinogen-treated surface (Fig. 1). When the retraction tension on the nerve is low, the stumps stick readily to this surface; the bond reaches its maximum effectiveness within approximately 10 minutes as the clot "sets."

6. The operation is completed by enveloping the stumps with the fibrin wrapping. The edges of the film may be brought around the stumps as shown in Fig. 2 or as in Fig. 3. Still another method of completing the envelopment is to place a second film, identically prepared, on top of the stumps and facing the first. This method may be of greater value where the nerve is flat and ribbon-like and when wrapping is difficult to perform. The edges of these two films are pressed together so that the nerve lies in an adherent envelope of adhesive film (Figs. 4 and 5). It is of great importance that the film, as it is applied, be kept as taut as possible at the level of the nerve wound. A kink or fold interposed between the stumps serves as an effective barrier to nerve repair.

MATERIALS

The materials used for end-to-end union of nerves, fibrinogen, thrombin, and fibrin film, were developed in the Department of Physical Chemistry, Harvard Medical School in the course of fractionation of human blood plasma and have been described elsewhere.[3,5,6]

The type of film employed in these studies contains the protein fibrin in highly concentrated form and a glycerol plasticizer which is readily replaced by water or saline upon immersion. Sheets of film from which appropriate lengths can be cut have been made available in a range of thicknesses characterized by the weight of fibrin per sq. cm. The 3-mg. film, used in most experiments reported here, is among the thinnest (approximately 0.1–0.2 mm.) of the films prepared, and differs with respect to several properties from the thick film that has been used successfully by Ingraham and Bailey[1,9] as a substitute for dura and by Michael and Abbott[10] as a wrapping around a damaged sciatic nerve.

The properties of the fibrin film that are of interest in connection with nerve suture may be recounted at the present time. The elasticity and pliability of the thin film has permitted intimate application under diverse conditions. The tensile strength has been sufficiently high to maintain apposition under conditions met in the present experiments. The transparency of the film has permitted continuous observation of the enclosed nerve throughout the operation. Of special value to the use of the film in nerve repair is its eventual complete resorption at rates that may be controlled by various procedures.[12]

Purified thrombin and fibrinogen have been made available in the dried state in small containers to which sterile water can be added aseptically. The solution of the fibrinogen fraction used in the present work contains approximately 2 per cent fibrinogen. When thrombin is added to this solution the fibrinogen clots, the rate of clot formation being controlled by the amount, expressed as units per cc., of thrombin added. A wide range in physical properties of the clot are obtainable, depending on salt concentration, pH, fibrinogen and thrombin concentrations.[6]

STUDIES OF THE TENSILE STRENGTH OF THE SUTURE LINE IN THE EXCISED SCIATIC NERVES OF RABBITS

Preliminary experiments on splicing of the sciatic nerve of living rabbits, utilizing the earliest prepared adhesives, demonstrated that the union was

too weak to ensure retention of the stumps. Consequently *in vitro* studies were undertaken directed towards the strengthening of the union by varying the method of application of film and clot.

To initiate the studies on excised nerves an approximate knowledge of the retraction stress on sciatic nerve stumps of the living rabbit was needed. This was obtained by recording *in vivo* the tension necessary to bring together the cut ends of the exposed sciatic nerve. With muscle retractors in place and the knee and foot flexed, the tension on the stumps was almost negligible, approximately 5 grams; whereas, with the limb in full extension, the stress was about 30 grams. These preliminary observations showed that in order to maintain continued apposition of the stumps, the strength of the union must surpass these values.

Following these preliminary observations the sciatic nerve of a rabbit was excised and cut into two pieces of equal length which were then reunited with film and clot. A standard time of 10 to 15 minutes was allowed following application of the film to ensure "setting" of the interposed clot, after which one stump was suspended from a spring balance by an attached thread. The opposite stump was pulled until the suture line was broken. The tension in grams was read directly from the spring balance by recording the maximum excursion of the reader. Each nerve, kept moist in saline solution between experiments, was used for 10 to 15 readings. Except for one series, the size of the fibrin sheet used was kept constant at 3 cm. in length ($1\frac{1}{2}$ cm. per stump) and $1\frac{1}{2}$ cm. in breadth. The method of application of film, fibrinogen and thrombin was varied until a significant rise in tensile strength of the union was observed. In this manner over 200 tensile strength readings were made.

In all cases the fibrin clot created between film and nerve proved to be the weakest link. The fibrin film and the nerve itself always withstood the highest tensions. Initial tensile strength readings averaged about 19 grams. Following the introduction of certain alterations in the procedure, it was possible finally to obtain unions capable of withstanding 195 grams tension. The method of application of film and clot that gave the latter readings was subsequently used with success *in vivo*. This method as elaborated *in vitro* is listed as the recommended procedure in the early pages of this work.

The factors of importance that influence the strength of the splice were mainly mechanical in nature. A thin fibrin film (3 mg.) provided a more effective union than a thicker one (6 mg.), an observation that indicated that a thin film by virtue of its pliability could be more intimately united with the nerve surface. Similarly, thin layers of fibrinogen were preferable to thicker ones since they afforded a more intimate union between nerve and film. When the film was partially dried before impregnation with fibrinogen, a remarkable increase in the tensile strength of the splice was obtained. A further notable rise was recorded when the surface of the nerve was made slightly dry before application of the film. Likewise, when dryness was maintained for about ten minutes after enveloping the stump with the film, dur-

ing which time the clot was forming, a stronger bond was invariably obtained. It is probable that drying facilitated the attachment of the clot to the surfaces of nerve and film. Another observation of importance emerged from *in vitro* studies in which different lengths of film were used. In these cases the tensile strength of the suture line was observed to bear a direct relation to the amount of surface of film and nerve in contact with one another. Therefore, longer strips of film are indicated where greater strengths are required.

Variations in the concentration of fibrinogen and thrombin were of little or no significance for the strength of the union. Low concentrations of fibrinogen proved as effective as higher ones. However, in the case of thrombin, there was a suggestion of greater strengths with lower concentrations.

APPLICATION OF THE FIBRIN-ADHESIVE TECHNIQUE TO NERVE SPLICING IN THE LIVING ANIMAL

Following its elaboration by means of the *in vitro* studies, the fibrin-adhesive technique was applied to the repair of the cut sciatic nerve of the rabbit. Experiments were designed to test the strength of the union *in vivo*, the reaction of the host tissue to the presence of the adhesive, and the nature of the nerve repair and nerve regeneration.

A. METHODS

Forty-two operations were performed on the sciatic nerves of young adult rabbits. In addition to these, certain other operations in which a less satisfactory method of application of the adhesive was utilized and some in which nerve resection followed by end-to-end union were performed are considered here.

The nerves were exposed under nembutal anaesthesia (0.65 cc./kg.) and ether using full aseptic precautions. The overlying muscles were separated along fascial planes. After division with sharp scissors, the nerve ends were brought into apposition with the fibrin-adhesive technique. The prevailing clinical procedure of close apposition of stumps was followed in most cases. In a few animals, however, the stumps were separated by a small gap. In most animals both sciatic nerves were used. Although care was taken to control the bleeding from the stumps, there were cases in which considerable oozing occurred after completion of the suture, the blood collecting between the film and the nerve surfaces. The stumps, nevertheless, retained their apposition during the postoperative period. Films of various persistence-times were employed in these experiments. The two-leaf or single-leaf method was used with equal success. The wound was closed with interrupted sutures in the skin and the animals were returned to their cages without immobilization of the paralyzed limbs.

At varying intervals after the operation the animals were again anaesthetized and the nerves carefully exposed for some distance above and below the suture. Notation was made of the position and of the condition of the nerve stumps and the fibrin wrapping. Some of the animals were killed in the early postoperative period for study of the tensile strength of the suture line, while others were used for estimation of the rate of fiber growth across the nerve wound. In the latter, the nerves were exposed during the second or third week after operation and the distance of fiber growth determined by the method of Gutmann, Guttmann, Medawar and Young.[7] At the end of the experiment the entire area involved in the suture, together with varying lengths of the distal stump, were removed and fixed (1 part formalin: 1 part glacial acetic acid: 18 parts 80 per cent alcohol). The remaining animals were opened and the nerves fixed at periods ranging up to five months after operation. Histological sections were stained by the Bodian silver method and counterstained with Mallory's triple stain or hematoxylin in conjunction with eosin, light green or Orange G.

B. RESULTS

Except for two of the forty-two cases the stumps retained their position following the operation. In one of the exceptions there was a partial retraction with a separation of 2 to 3 mm. between the stumps; in the other the separation was much more extensive.

The extent of adhesion of the sutured nerve to the surrounding tissues varied considerably. In no case was the adhesion heavy. Ordinarily one side of the nerve was adherent to the adjacent muscle by growth of connective tissue, while the opposite side remained relatively free. In a few cases the entire suture area was free of any marked adhesions (Fig. 6). Edema of the stumps (refer to Weiss' recent discussion[19]) varied in intensity (Figs. 6, 7, 8, 10, 11, 17, 22 and 26) in different animals.

During the early postoperative days the film was clearly evident and had retained its position in relation to the nerve. Where a wing had been present, as after the application of the film in the procedure shown in Figs. 3 and 4, it was rolled up or pushed against the nerve because of the action of the adjacent muscles (Fig. 17).

No systematic studies have been made on functional return. However, three animals observed after four to five months following operation showed signs of return of sensitivity and motility of the foot.

1. *The Tensile Strength of the Suture Line.* Since films of different persistence-times are available, some estimate is required of the length of time that the film need remain intact until adequate healing of the cut ends of the nerve would ensure continued apposition of the stumps. Although rapidly absorbable films have been used with success in many operations reported here, they may prove inadequate under conditions more exacting in terms of tension. Indeed, the only total failure of the forty-two splices described in the present paper was one in which a film of low persistence-time was used; the film broke during the very early postoperative days.

The present section is devoted to an analysis of changes in the tensile strength of the suture line in order to define more accurately the requirements of the adhesive. The results of these experiments are depicted in graphical form in Fig. 9. The tensile strength of the union remained approximately constant during the first three postoperative days but dropped by the fourth day to an average of 90 grams. Thereafter it rose continuously and rapidly to an average of 338 grams on the sixth day and 625 grams on the tenth. The latter two values demonstrate that sufficient healing occurred by the end of the fifth or sixth day to ensure retention of the stumps without the aid of the suture material. The data obtained in the present experiments compare well with those of Miller[11] who studied the changes in tensile strength of the suture line in weekly intervals beginning with the first week following suture of the divided sciatic nerve of the dog with catgut or silk.

The manner in which the stumps separated at the limiting tension revealed that a decided drop in the tensile strength of the film occurred during the early postoperative period. Indeed, the film at this time proved to be the weakest link in the union. These results differ from those obtained *in vitro*

where the strength of the film always surpassed the limiting strength of the union. Even after the first day *in vivo*, at a time when there could have been no marked drop in weight of the film,[12] the tensile strength of the suture line (average, 125 grams) was far below the values that the film exceeded *in vitro*. In contrast to the rapid loss in strength of the film *in vivo* was the increased firmness of the bond between the film and the nerve. When attempts were made to lift the film from the surface of the nerve, it invariably tore before separation occurred.

When tension on the stumps is negligible, considerations of tensile strength need not determine the type of film to be selected. Under more

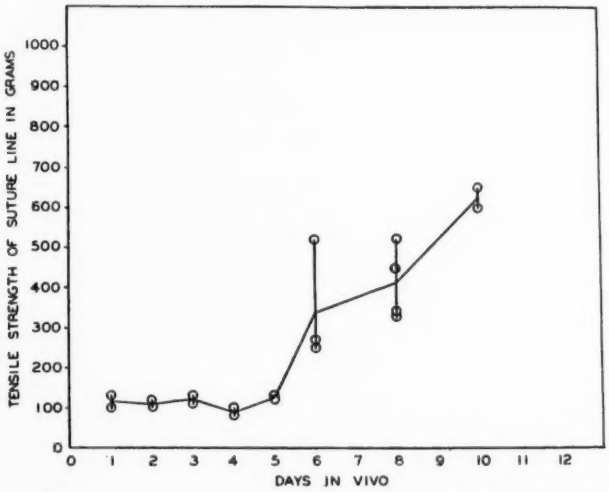


FIG 9. Change in the tensile strength of the suture line during the early postoperative days.

exacting conditions, a film that will retain its strength during approximately the first week after operation is most desirable since it will ensure continued apposition of the stumps. Whether such a film can be prepared without introducing certain disadvantages, such as increased tissue reaction, is not known.

2. *Delay of Neuronal Regeneration at the Suture Line.* The latent period which previous workers have noted prior to the appearance of regenerating fibers in the distal stump has been estimated in the rabbit with various methods of suture at 7 to 8 days.[2,7] This delay has been attributed to ascending or traumatic degeneration of the fibers of the proximal stump followed by their regeneration to the level of the wound and their subsequent growth through the scar. In order to test the influence of fibrin adhesive upon this latent period, the distance of growth of fibers through the distal stump was measured 13 to 20 days after operation in a series of rabbits. From these readings the delay was calculated by assuming a constant rate of neuronal

growth in the distal stump of 3.5 mm./day, the value obtained by Gutmann, Guttmann, Medawar and Young.[7] The results observed in eleven instances are shown in Table I. The variability in the calculated delay is probably due to individual variations in the rate of growth through the distal stump and to slight differences in the extent of apposition of the stumps. The average delay is 6.9 days which compares favorably with the estimates obtained by previous workers using other techniques.

3. *Histological Observations of the Repair of Sutured Nerves.* The histological material, ranging up to 5 months after operation, showed that nerve fibers had grown in abundance across the wound area. However, the arrangement of the regenerated fibers in the wound region varied among the cases

TABLE I

Delay of regenerating fibers before entering distal stump

Days after operation	Recorded distance of growth through distal stump (mm.)	Days of growth in distal stump (distance divided by rate of 3.5 mm./day)	Initial delay in days (days after operation minus days of growth)
20	56.0	16.0	4.0
20	54.0	15.4	4.6
20	37.0	10.6	9.4
20	34.0	9.7	10.3
19	51.0	14.6	4.4
19	44.0	12.6	6.4
19	41.0	11.7	7.3
19	40.0	11.4	7.6
19	40.0	11.4	7.6
19	37.0	10.6	8.4
13	25.0	7.1	5.9
			Average = 6.9

observed. In the most favorable instances (Figs. 10 to 15) the nerve fibers were mainly oriented along the length of the nerve with only the smallest local deviations from a direct course. The occasional irregularities of growth observed in these cases (Fig. 15) were not confined to any particular portion of the junctional tissue—in some being located centrally, in others peripherally. In the most unfavorable cases there was extensive wandering and crisscrossing of fibers (Fig. 16). The average cases were those in which the growth of the nerves was predominantly uniform but exhibited local areas of irregular orientation. Histological observations showed that irregular growth of nerve fibers was probably due to factors other than the presence of the adhesive.

A notable cause of irregular regrowth of nerve fibers in the wound region was related to the slight evulsion or protrusion of the cut nerve end resulting from a retraction of the surrounding epineurium greater than that of the enclosed nervous tissue. The evulsion took the form of a cone with the medially located nerve fibers protruding from the cut epineurium for a greater distance than the marginal fibers (Fig. 17, note proximal tibial stump). The

central fibers retained their longitudinal orientation while the more lateral fibers were bent outwards. As shown in Fig. 18, these lateral, outwardly directed, fibers encountered, as they grew, the proliferating fibrous tissue subjacent to the fibrin film, as a result of which some have become recurrent, others have become lost in the maze of connective tissue, while the remainder, following an irregular course, have grown toward the distal stump. At the apex of the cone, where the fibers are oriented along the axis of the nerve, regrowth of fibers has taken place in a straight line (Fig. 19). It is possible that resection of the evulsed cone-shaped area of the stumps at the time of operation would be more conducive to a uniform and parallel orientation of neuronal regeneration.

Another cause of irregular growth which appeared in the study of sections was telescoping or flanging of the nerve ends at the time of operation as a result of close apposition of the nerve ends. In some cases apposed nerve funiculi were pressed so closely against each other that they were deviated laterally (Fig. 20) or bent backward (Fig. 21), resulting in a subsequent disoriented regeneration of nerve fibers. Another example of telescoping as a result of close apposition is shown in Fig. 22 where the proximal peroneal stump is telescoped between the distal peroneal and tibial stumps.

A more orderly regeneration was invariably observed when telescoping or flanging was avoided. In a few instances where the stumps were separated by small gaps rather than closely apposed, these gaps (1 to 4 mm.) were invaded by regenerating nerve tissue which was invariably oriented parallel to the length of the nerve (Figs. 23 to 26). The only growth irregularities observed were found at the junction between the bridge of regenerated tissue and the ends of the stumps; these irregularities probably arose as a result of the above-described disorienting effects of the evulsed nerve substance. The orderly arrangement of the fibers in the bridge of regenerated tissue observed here agrees well with the results obtained by Weiss and Taylor,[22] who used the arterial splice in a detailed analysis of mechanical factors involved in the repair of nerves. They recommend separation of the stumps by a small blood-filled gap rather than close apposition. Weiss and Taylor also observed a reunion of the stumps in a few cases in which the stumps were more extensively separated. A similar result was obtained in two cases of the early experiments with the fibrin-adhesive splice. The stumps retracted during the postoperative period leaving a gap of 10 to 12 mm. which was later bridged by a well-oriented growth (Fig. 27). Due, in part at least, to collapse of the film, the gap was reduced laterally thereby limiting the volume of regenerated tissue.

4. *Histological and Pathological Studies of the Fibrin Film.* Attention was directed in these studies to the fate of the film, the extent of tissue reaction and the relation of the film and surrounding reaction to the nerve.

Rapid initial absorption of the film resulted by the fifth or sixth postoperative day in its fragmentation (Fig. 28). The remnants, large at first, were rapidly reduced in size, many disappearing entirely within the next few

days. By the twentieth to thirtieth day most of the film had been resorbed aside from occasional small fragments which stained very deeply and were found even after 112 (Fig. 29) and 155 days (Fig. 22).

The film gave rise to a fibrous and cellular reaction which was not pronounced initially (7 to 10 days) but increased to a maximum at about 20 to 30 days. This reaction declined progressively until by 155 days it was evident in diminished amount around the small remaining fragments of film (Figs. 22 and 29). The cellular reaction was mainly in immediate contact with the film; the fibrous reaction, while intermingled in part with the cellular, was concentrated more on the periphery and oriented tangentially to the film.

The character of the cellular reaction showed a continuous sequence of change. A small number of polymorphonuclear leukocytes was present during the very early days and in close association with the film (Fig. 30). During the early days cells containing an oval nucleus and abundant clear cytoplasm were also present, but from about the seventh day onward began to disappear slowly in favor of increasing numbers of multinucleate giant cells. The latter, which often completely encapsulated the fragments of film (Fig. 31), appeared to assist in digesting the fibrin. Following resorption of the film, the giant cells disappeared. A lymphocytic infiltration was also noted but was of irregular occurrence, being especially apparent in some regions and not in others. Where present, it was especially intense between the fifteenth to fiftieth days and was located mainly within the inner layer of the fibrous encapsulation. The lymphocytic reaction also subsided as the film was resorbed.

The fibrous reaction, which consisted during the early days of a loose irregular connective tissue abundantly supplied with small vessels (Figs. 28 and 30), later became organized to form a definite capsule (Fig. 31). The extent of fibrous encapsulation varied from one animal to another, being pronounced in some and not in others. The differences may well be due to differences in the film; further standardization is required. Although more prolonged experiments are indicated at present, there was no evidence over four to five month periods of strangulation of the nerve due to contraction of the encapsulating fibrous tissue.

Of particular importance in the histological study was the relation that the film and its surrounding reaction bore to the nerve. Since a detailed study of the very early stages of repair was not made, influence of the early reaction on nerve repair was not determined. From study of later stages, however, it appeared in general that the film and its surrounding reaction were confined to the periphery without interference with union of the stumps (Figs. 10, 11, 17, 22, 26 to 29). Invariably, there was a definite line of separation between reaction tissue and nerve. In one case, however, in which a kink of film had been inadvertently inserted between the stumps at the time of operation, fibrosis effectively prevented nerve regeneration of that region of the junction.

Although no experiments have been performed to compare the extent of reaction to the adhesive with that to other suture materials, a rough comparison with the results of other workers showed that tissue reaction to the film was more extensive than to other materials that have been recently recommended as highly favorable, for example: hair suture (Guttmann, 1943), homologous or autologous plasma (Tarlov, 1943), homoplastic arterial splices (Weiss, 1943), and tantalum wire (Spurling, 1944). The interference of the film with nerve repair may be much less than that of hair, tantalum, or plasma suture, since the film is confined to the periphery and is not inserted into the nerve tissue or between the stumps. However, search must be made for a film or other membrane which would compare favorably in reaction to such materials as tantalum and hair before specific recommendations can be made for clinical use.

COMMENT

A notable advantage to the use of the fibrin adhesive is that of technical simplicity. No special instruments or skill are required. The film is very easy to apply where tension on the nerve is low. However, unlike thread suture of nerves, the fibrin adhesive does not develop its full binding strength until full envelopment of the film has been accomplished and the clot has "set." Therefore, under tensions greater than those observed in primary suture of the rabbit sciatic, difficulty may be encountered in keeping the stumps apposed while the suture is completed. In that event temporary stay sutures may prove of value.

The values achieved by the *in vitro* studies by no means exhaust the possibilities for increasing further the tensile strength of the suture line of nerves united with the fibrin adhesive. The *in vitro* studies have shown that some of the factors that allow for greater tensile strengths are physical ones such as dryness of the film and stumps, thickness of the layer of fibrinogen between nerve and stumps, and thickness and length of the film. Future variations in the mode of application of film and clot may prove equally significant. Alteration of the pH of the fibrinogen solution (Ferry and Morrison[6]) and study of the film with a view towards increasing its strength during the postoperative days may deserve further investigation.

There are advantages other than ease of application to the use of the fibrin adhesive. The transparency of the film permits continuous observation of the suture line during the operation. The film is elastic and gives readily with movement of adjacent tissues, thus minimizing the strain on the nerve. The adhesive, when properly applied, is in contact only with the epineurium, and no extraneous or foreign material is interposed between the stumps. The method may be varied in many directions to suit special requirements, and may be adapted to a variety of conditions including the repair of partially severed nerves.

Additional work is required to select the fibrin film best suited in terms

of tensile qualities and extent of tissue reaction evoked before the fibrin adhesive can be recommended for clinical use. Furthermore, it may yet emerge that membranes other than fibrin film will prove best suited to the many potential uses of a general biological adhesive in neurological and other branches of surgery.

During the course of analysis of the fibrin-adhesive method, observations of interest were accumulated on other aspects of nerve repair. Notable among these were observations on the change in tensile strength of the suture line during the early postoperative days. A firm union of the apposed stumps is obtained within the first week following operation. By the tenth day the tensile strength of the union had risen to a value far surpassing that which is initially obtained with the use of any suture material. Thus a suture material that is designed merely to retain the union of the stumps is of little value beyond approximately the first to second week after operation. The remarkable rise in tensile strength beginning with the fifth postoperative day may be correlated with the outflow of Schwann cells and fibroblasts which occurs from the stumps at this time.[22] During the ensuing days, as collagen fibers are formed and as nerve fibers cross the wound into the distal stump, the strength of the union is further increased. In addition to uniting the two stumps, the arrangement of the cellular material also forms the pattern for subsequent bridging of the union by regenerating nerve fibers.[22]

A study of the delay before regenerating nerve fibers reach the distal stump has also been made in the analysis of the adhesive. The results of this study support those obtained previously by Gutmann et al.[7] using other methods of nerve reunion. Following close approximation of the nerve ends, about seven days are required for regenerating fibers of the proximal stump to reach the distal.

SUMMARY

A method of uniting nerve stumps without the use of thread sutures is described in the present work. The technique, designated as the *fibrin-adhesive method*, involves the use of a thin smooth film of fibrin prepared from products of fractionation of human blood plasma. The film is impregnated with thrombin, surfaced with fibrinogen, and then applied to the apposed nerve stumps by one of several methods (text Figs. 1 to 5). The fibrinogen as it clots binds the film to the surface of the nerve and thus serves to transmit the stress of retraction of the stumps to the film. In addition to maintaining apposition of the stumps, the film serves as an envelope enclosing the nerve stumps and nerve wound in a continuous channel. The fibrin-adhesive method of nerve splicing has the advantages of simplicity of application and of introducing no extraneous materials or obstacles to growth into the nerve trunks themselves or between the stumps. The film is transparent and consequently allows for continued observation of the nerve stumps throughout the operation.

The major portion of the present work presents the results of *in vitro* and *in vivo* studies of the tensile strength of the suture line, together with histological observations on the resorption of the film, on the character of the nerve regeneration and on the nature of the tissue reaction to the presence of the film in rabbits.

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PLATE I

FIG. 6. *A27L*. After 155 days. End-to-end union following 3-mm. resection of nerve. Note the absence of any marked adhesions. Refer also to Fig. 22. C.N.S., central nervous system; S, suture line. × approximately 1.

FIG. 7. *A26L*. Fixed after 65 days. C.N.S., central nervous system; S, suture line. × approximately 1.

FIG. 8. *A37R* and *L*. Fixed after 65 days. Note excellent union. C.N.S., central nervous system; S, suture line. × approximately 1.

FIG. 10. *A37R*. After 65 days. Refer also to gross appearance in Fig. 8. Note excellent union between stumps. The dark area in upper right part of nerve is an excessively stained region. C.N.S., central nervous system; S, suture line. Stain: silver, Orange G. ×4.5.

FIG. 11. *A37L*. After 65 days. Refer also to gross appearance in Fig. 8. Note excellent union between stumps. The dark area in upper right part of nerve is an overstained region. C.N.S., central nervous system; S, suture line. Stain: silver, Mallory. ×4.5.

FIG. 12. *A33R*. After 20 days, showing straight-line orientation and abundant growth of nerve fibers in union tissue between stumps. Stain: silver, hematoxylin, light green. ×135.

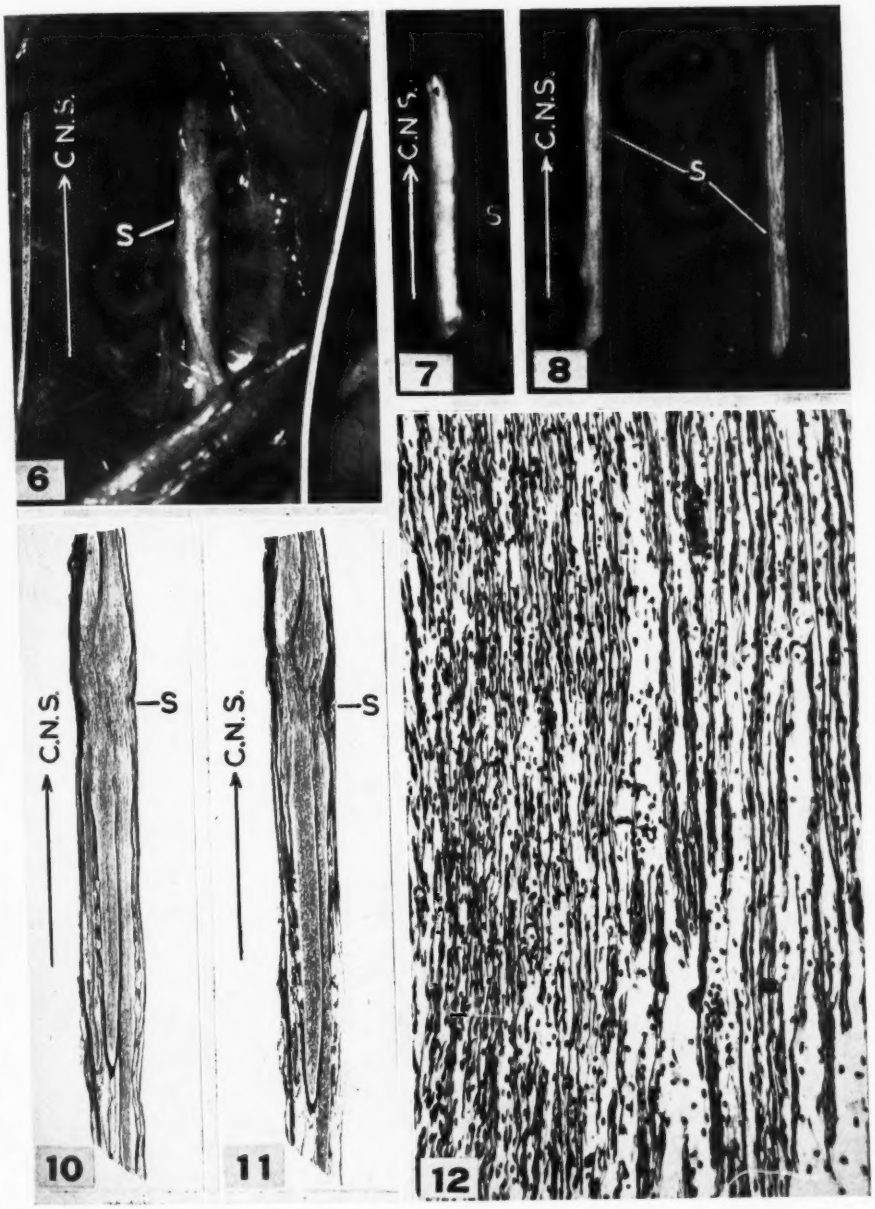

PLATE I

PLATE II

FIG. 13. *A33L*. After 20 days, showing straight-line orientation of nerve fibers in junction tissue. Stain: silver, hematoxylin, Orange G. ×340.

FIG. 14. *A39L*. After 19 days, showing straight-line growth across junction between proximal and distal stumps. U, union tissue. Stain: silver, hematoxylin, eosin. ×45.

FIG. 15. *A3R*. After 13 days, showing the character of the disorientations observed at the suture line in the best cases. Note the abundance of nerve fibers. Stain: silver, Orange G. ×200.

FIG. 16. *A35L*. After 14 days, showing irregular orientation of fibers and union tissue between stumps in the worst cases. Stain: silver, hematoxylin, light green. ×200.

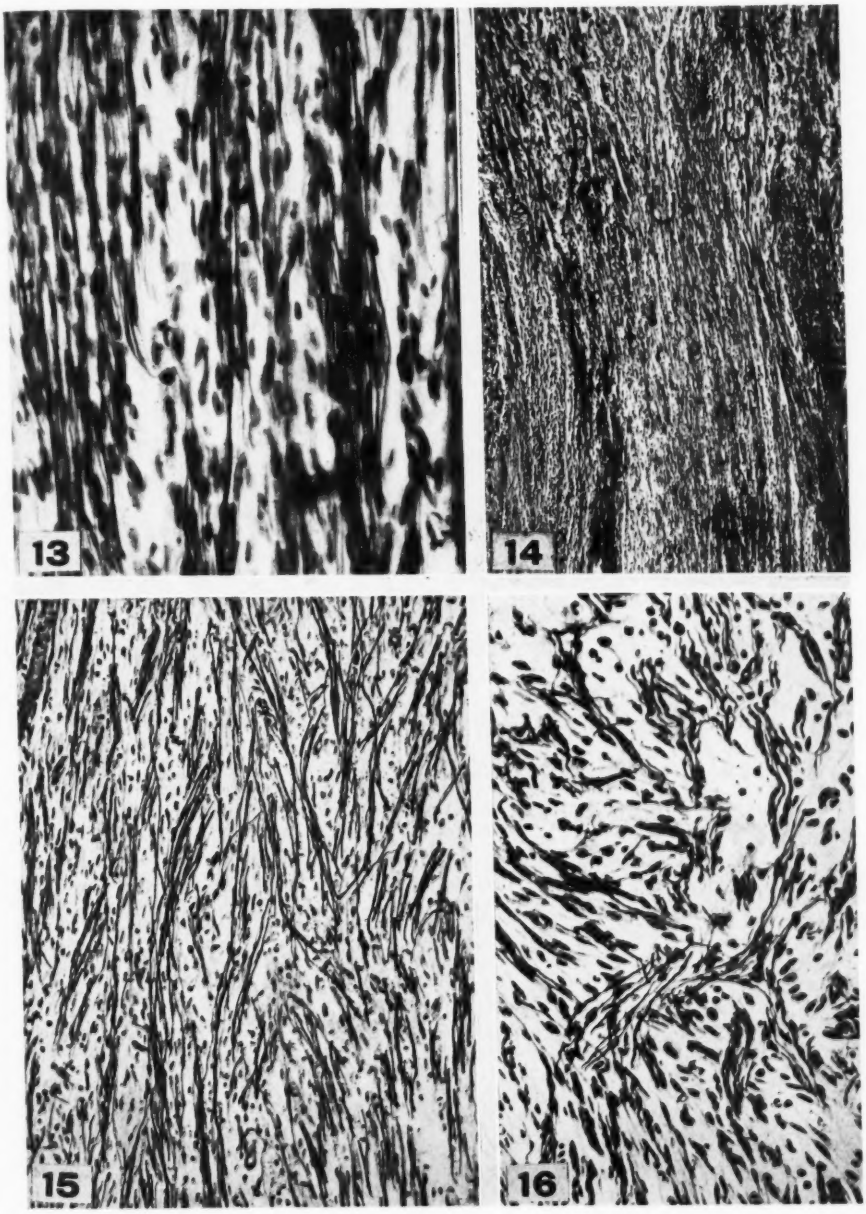

PLATE II

PLATE III

FIG. 17. *A39R.* After 19 days. Note conical evulsion of nerve substance from epineurium of proximal tibial division, the wing of film rolled up and pressed against the nerve, and the position of the film and surrounding reaction tissue in respect to suture line. C.N.S., central nervous system; F, film; E, cut end of epineurium. Stain: silver, Orange G. ×4.5.

FIG. 18. *A39R.* After 19 days. Higher power view of evulsed proximal tibial stump of Fig. 20 to show lateral growth of fibers and entanglement in surrounding connective tissue. Stain: silver, Orange G. ×80.

FIG. 19. *A39R.* After 19 days, showing straight-line central growth from apex of conical evulsion. Refer also to Figs. 17 and 18. Stain: silver, Orange G. ×80.

FIG. 20. *A29L.* After 7 days, showing results of telescoping of stumps during apposition. Note lateral deviation of fibers of proximal stump. Stain: silver, hematoxylin, light green. ×135.

FIG. 21. *A39R.* After 19 days, showing another cause of irregular growth following close apposition of stumps. The sural division of the sciatic is bent back on itself. Stain: silver, Orange G. ×80.

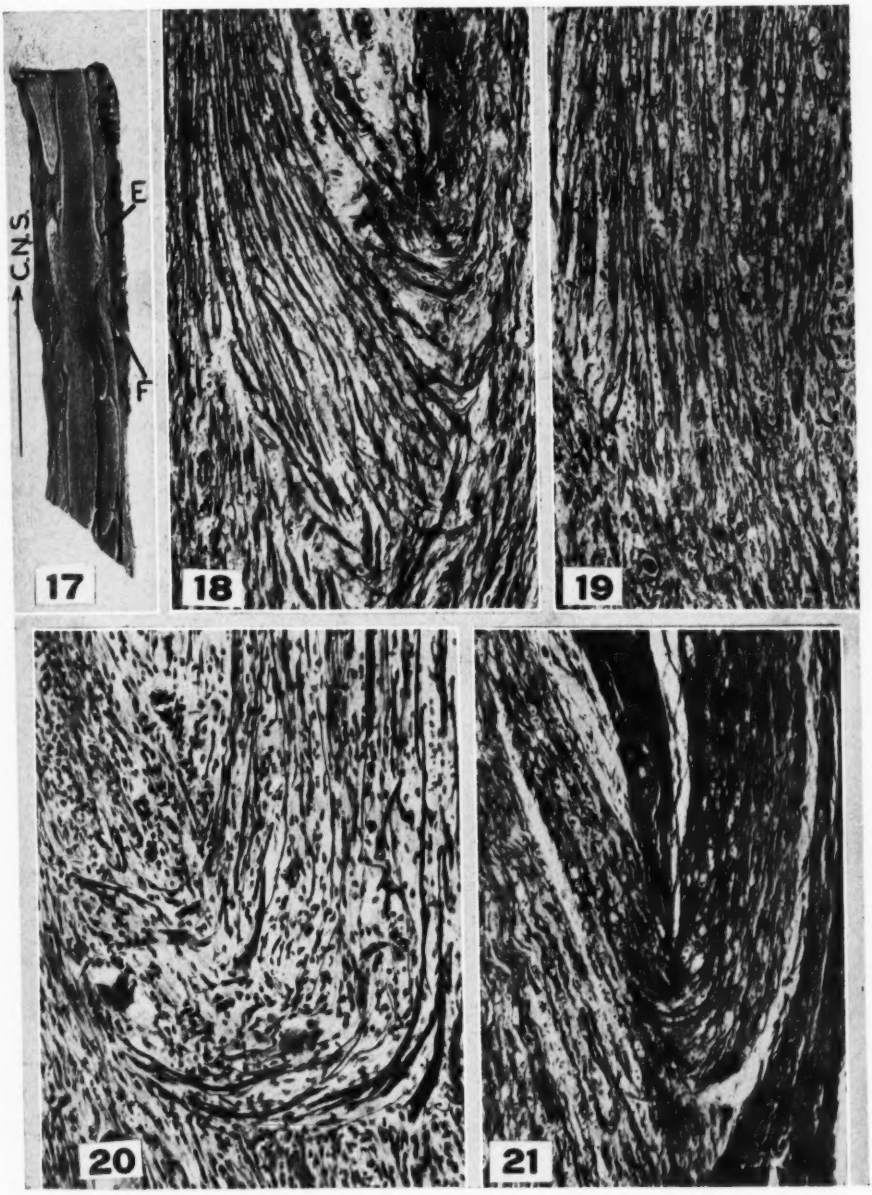

PLATE III

PLATE IV

FIG. 22. *A27L.* After 155 days. Note poor alignment of peroneal stumps as a result of close apposition; straight-line growth between tibial stumps; small fragments of film that remain on the periphery; and absence of any marked fibrosis or any involvement of reaction tissue in junctional tissue. Refer also to gross appearance, Fig. 6. C.N.S., central nervous system; F, film fragments; P, peroneal nerve; T, tibial nerve. Stain: silver, Orange G. ×4.5.

FIG. 23. *A7R.* After 34 days, showing growth within former gap region of 1 mm. Note straight-line growth of nerve fibers. Stain: silver, Orange G. ×400.

FIG. 24. *A4L.* After 112 days, showing regenerated nerve within former gap of 4 mm. Note fasciculation and general proximodistal orientation of fibers. Refer also to low power view, Fig. 26. Stain: silver, hematoxylin, light green. X135.

FIG. 25. *A10L.* After 31 days, showing union tissue within former gap of 2 mm. Note the abundance and the parallel orientation of regenerated fibers. Stain: silver, Orange G. ×135.

FIG. 26. *A4L.* After 112 days. Union tissue between stumps separated by 4 mm. Note straight-line growth of fibers and absence of film. Refer also to high power view, Fig. 24. C.N.S., central nervous system; x, knife scratch. Stain: silver, hematoxylin, light green. ×4.5.

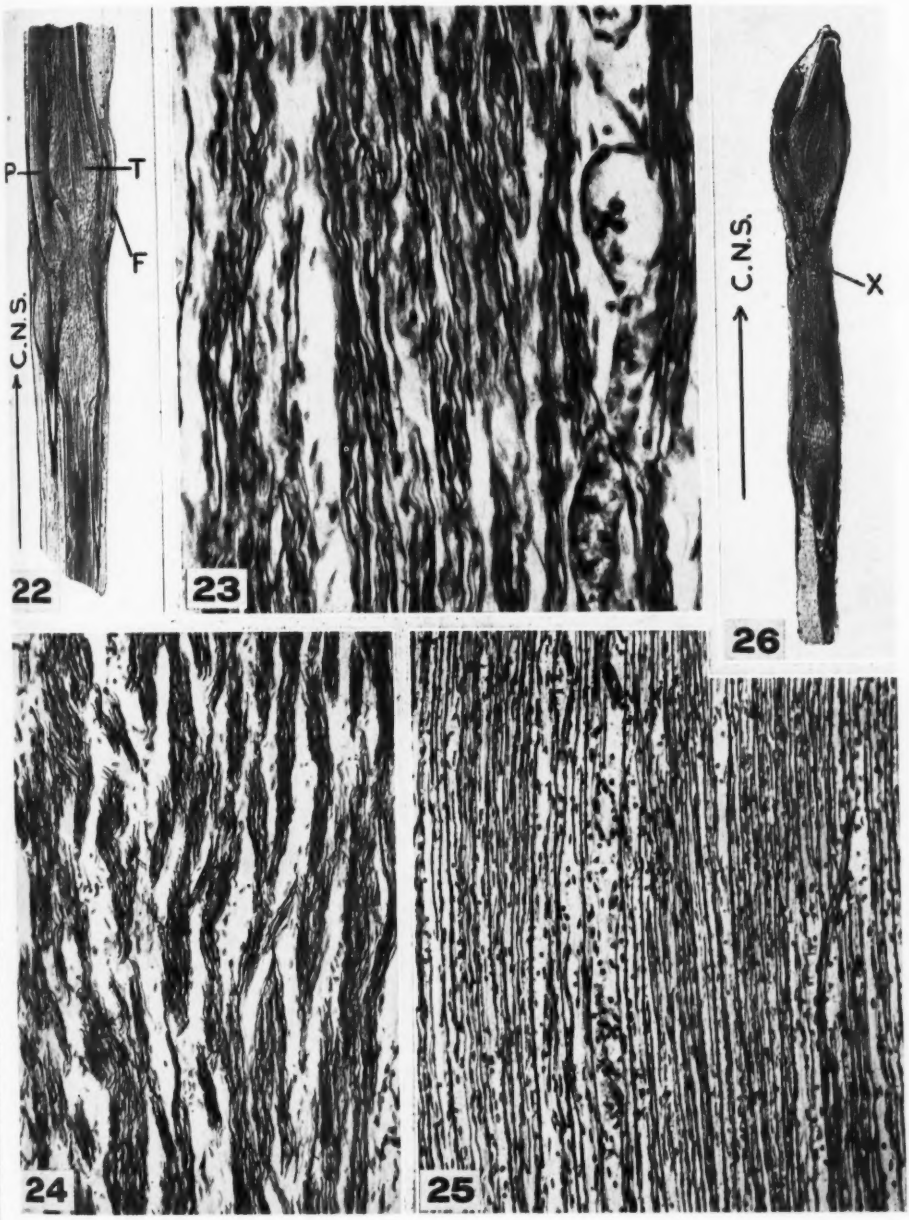

PLATE IV

PLATE V

FIG. 27. *A9R.* After 34 days, showing regeneration from proximal stump following retraction of stumps and separation by a 10-mm. gap. Film, except for small fragments, removed prior to sectioning. Note bottleneck created by collapse of film; parallel orientation; and abundant growth of fibers. P, proximal stump; F, film fragments. Stain: silver, Orange G. ×45.

FIG. 28. *A28L.* After 5 days, showing condition of film and relation to nerve. Note fragmentation of film and the fibrous and cellular reaction encapsulating it. N, nerve; F, film. Stain: silver, hematoxylin, light green. ×80.

FIG. 29. *A4R.* After 112 days showing small film fragment and its relation to nerve. Note absence of any marked reaction and position of film on periphery of junctional tissue. F, film fragment; N, nerve. Stain: silver, hematoxylin, light green. ×340.

FIG. 30. *A16R.* After 4 days, showing reaction to film. Note small number of polymorphonuclear leukocytes, scattered and irregularly oriented fibroblasts and abundance of small vessels. F, film. Stain: silver, hematoxylin, light green. ×340.

FIG. 31. *A7R.* After 34 days. Film fragment completely encapsulated by giant cells; fibrous tissue on the periphery. Note relation of cytoplasmic processes of giant cells to surface corrugations of the film. G.C., giant cells; F, film fragment; F.C., fibrous capsule. Stain: silver, Orange G. ×200.

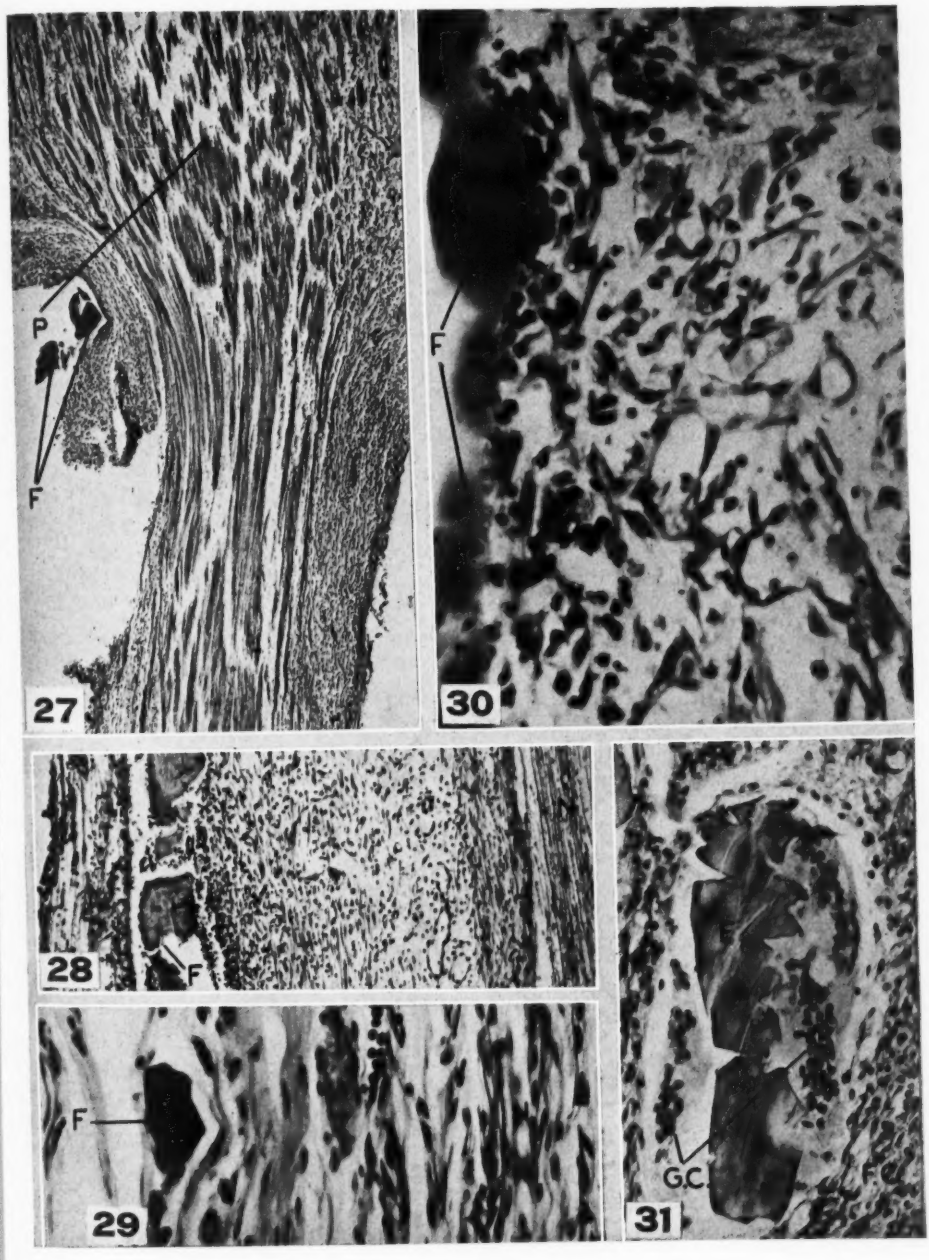

PLATE V

UNUSUAL SIZE AND EXTENSION OF A PITUITARY ADENOMA

CASE REPORT OF A CHROMOPHOBE TUMOUR WITH UNUSUALLY EXTENSIVE COMPRESSION OF THE BASE OF THE BRAIN, AND REVIEW OF THE LITERATURE ON THE PATHWAYS OF EXTENSION OF THESE TUMOURS

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OWING to their classical symptoms, adenomas arising from within the sella turcica are rarely permitted to attain any considerable growth before being submitted to operation. This is particularly true of the secreting chromophil adenomata,* but the chromophobe variety may grow to a very large size and, in cases of unusual fixation of the optic chiasm, may do so without compressing the decussating optic fibres.[9] In the rare instances where operation has been overlong deferred these neoplasms tend to extend into unusual areas, with the result that diagnosis may become a difficult problem and the predominant symptoms may lead to operation directed against the extension rather than the primary growth. These parasellar extensions not only produce profound alterations in the characteristic clinical syndrome, but complicate the surgeon's task to a degree where his operative mortality may become prohibitive. In Dr. Harvey Cushing's series of 338 adenomas (as reported by Henderson[8]) and in Jefferson's[9] 128 cases, some degree of unusual extension into the parasellar structures occurred in as high a ratio as 22 per cent of the former and 14 per cent of the latter.

To judge from the scarcity of published clinical reports, little attention has been paid to this potential danger. Such complications may result either from failure to establish an early diagnosis, overenthusiastic and prolonged attempts to control the growth by radiation, or procrastination on the part of the physician. Cushing[4] mentioned only 2 specific examples and Henderson,[8] in his detailed study of 338 pituitary tumours operated upon by Dr. Cushing, devoted little space to them and mentioned only four pathways of extension. A brief reference to these unusual extensions in Dr. Cushing's cases is also made in the survey of the Brigham series made by Dott and Bailey.[6] By far the most important paper on this subject was given by Jefferson[9] in 1940 in his President's address before the Royal Society of Medicine. Unfortunately this article has been published only in the Proceedings of the Society, so it can have come to the attention of but few medical readers in this country. Jefferson cites three main factors in the production of extrasellar extensions: (a) the growth urge of the adenoma, (b) the state of fixation of the chiasm, and (c) the shape of the pituitary fossa and the nature

* Even the chromophil adenomata may, on very rare occasions, reach a large size and extend into unusual areas, as occurred in a patient of Dr. Cushing's reported by Dott and Bailey.[6]

of its diaphragm. His paper should be read by all who have to deal with these tumours and are interested in the mechanism of their spread.

Six possible pathways of extension have been found at operation or post mortem after the expanding adenoma has escaped the usual boundaries of the pituitary fossa:

(1) *Pharyngeal extension*: The commonest pathway of growth is downward by bony absorption of the sellar floor, so that the tumour expands into the sphenoid sinus. This situation has long been recognized, as it is easily diagnosed by x-ray. As tumour extension into this area involves no important structures, it produces no outstanding clinical signs unless erosion continues into the nasopharynx. The patient is then likely to complain of discharge and increasing nasal obstruction. A mass can usually be visualized in the roof of the nasopharynx. According to Henderson[8] there were 8 of these complications in Dr. Cushing's series. Bailey and Cutler[2] have recently described such a case where nasal obstruction was the predominant symptom. Resection and biopsy of a "nasal polyp" revealed a chromophobe adenoma of pituitary origin. This woman had unusually extensive destruction of the sella, and at necropsy the tumour was found to have eroded through its floor and the sphenoid sinus directly into the nasal cavity. From its microscopical appearance this tumour was classified as a malignant adenoma. Extensive erosion and rupture into the nasopharynx have also been observed in rare cases of carcinoma of the pituitary, which have been summarized by Ewing.[7]

(2) *Hypothalamic extension**: This is caused by projection of the tumour directly upwards into the third ventricle behind a prefixed chiasm, as is so frequently the case with craniopharyngiomas. Here the usual symptoms, apart from visual disturbances, are headache and drowsiness, with possible evidence of injury to the autonomic centres. Jefferson points out that temperature variations and cardiac or respiratory alterations are not common with tumours that merely indent the hypothalamus without actually invading its walls, but polydipsia and polyuria may be produced by involvement of the supraoptico-hypophysial tract. Since tumour filling the third ventricle blocks the outflow of the cerebrospinal fluid, headache of the severest type with papilloedema may occur in this variety.

(3) *Temporal extension*: A lateral escape of tumour cells between the optic chiasm and the cavernous sinus may result in proliferation of the growth in the middle fossa. It will then compress the optic tract and the medial portion of the temporal lobe. This will result in an homonymous hemianopsia, and frequently in Jacksonian seizures preceded by an olfactory aura. Striking examples are illustrated in Cushing's book[4] and in the more recent articles of Vosskühler[14] and Jefferson.[9]

Henderson[8] has also mentioned a possible extension into the sylvian fissure, in which the adenoma grows laterally but in a more upward direction

* This is classified as "thalamic extension" in Henderson's paper, but Jefferson's preference for hypothalamic seems more logical.

than in the typical temporal expansion. He claims that it may thereby destroy the optic nerve. Compression of the frontal and temporal lobes would lead to mental deterioration, seizures with olfactory hallucinations, hemiparesis, and death from increased intracranial pressure (usually, as he pointed out, before vision is lost in the nasal field of the contralateral eye). Jefferson[9] doubts the existence of a true sylvian extension as a solitary feature, and no actual example was described by Henderson.

(4) *Invasion of the cavernous sinus*: Tumours that invade the cavernous sinus and Meckel's cave have usually broken out of their capsule and taken on certain malignant characteristics, although the tumour cells may still retain a cell type similar to that of the smaller tumours. Jefferson[9] has classified them as "malignant adenomata." When there is invasion of the cavernous sinus, certain classical signs result from compression of the structures that it contains, and there may be further lateral extension with stripping of the dura from the floor of the middle fossa and invasion of the trigeminal root sheath (Meckel's cave). Dott and Bailey[6] in their review of Dr. Cushing's cases recorded 2 particularly striking examples. In one the tumour spread beneath the dura all the way across the middle fossa, eroded the squamous portion of the temporal bone, and appeared outside the cranium beneath the temporal muscle. In the other, the growth surrounded the extradural portion of both internal carotid arteries. An excellent account of tumour invasion of the cavernous sinus has been presented by Weinberger, Adler, and Grant,[15] who described 14 examples from a series of 169 cases of verified hypophysial adenomas in the collection of the Hospital of the University of Pennsylvania. Invasion of the cavernous sinus may be diagnosed from the resultant disturbances of the structures that it contains—palsies of the nerves to the muscles of the eye, irritation of the ophthalmic division of the trigeminal, and engorgement of the orbital veins.

The two remaining pathways of extension are the rarest varieties of adenomatous outgrowth:

(5) *Posterior subtentorial extension*: Examples of extension backwards and downwards beneath the tentorium into the cerebellopontine angle are to be found in Cases 3 and 5 of the series presented by Weinberger, Adler, and Grant. In Case 5 the diagnosis lay between an hypophysial tumour, based on the roentgen findings, or a tumour of the cerebellopontine angle, suggested by the erosion of the petrous tip, cerebellar signs, and unilateral paralyses of the third, fifth, sixth, and eighth cranial nerves. There were in addition bilateral papilloedema, reduced acuity of vision, and absence of any field defect. This led Dr. Charles Frazier to explore the posterior fossa. The patient died soon after the operation, and a post-mortem photograph of the brain shows that the tumour, a chromophobe adenoma, had extended laterally to surround the cavernous sinus and gasserian ganglion. A portion had also extended backwards beneath the tentorium into the posterior fossa to occupy its right cerebellopontine angle (Fig. 1).

(6) *Frontal extension*: An equally rare pathway of extension is upwards and forwards, so that the tumour either escapes from beneath a post-fixed chiasm or actually surrounds this structure. When the tumour has made its escape in this direction, it extends along the floor of the anterior fossa, separating and compressing the frontal lobes. After going through the Quarterly Cumulative Index from its first volume in 1916 to the present, we have been able to find only 4 cases of this type on record. The first was reported by Müller.[10] His 62-year-old patient had a seven-year history of progressive

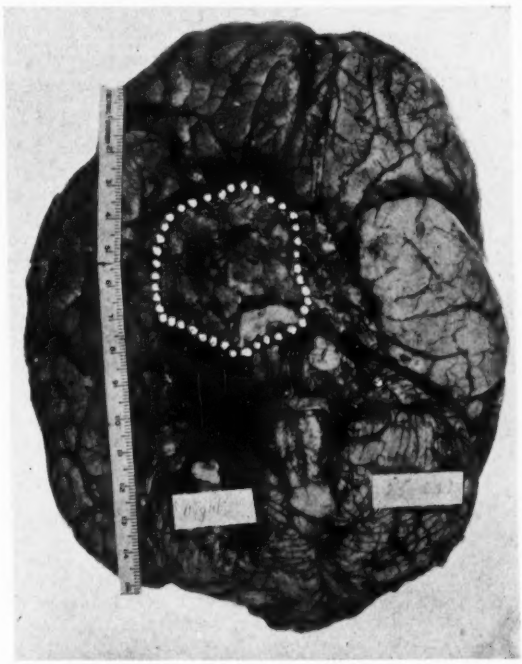

FIG. 1. Chromophobe adenoma from the collection of the University of Pennsylvania Hospital, reported by Weinberger, Adler, and Grant.[15] This tumour had extended downwards beneath the tentorium, producing symptoms simulating an acoustic neuroma. Tumour outlined by white dotted line. (Reproduced by courtesy of *Archives of Ophthalmology*.)

blindness leading to optic atrophy and finally death from bronchopneumonia. The clinical data on this case are meagre, but there is no mention of seizures or change in personality. Post-mortem examination disclosed a "hen's egg"-sized chromophobe adenoma, which originated in the sella and compressed the optic and olfactory nerves (Fig. 2). The frontal lobes and corpus callosum were compressed, the septum lucidum and fornix pressed to the left. The tumour encroached upon and was adherent to the floor of the anterior horn of the left lateral ventricle. Jefferson[9] has added 3 more

cases, in which the patients had epileptiform seizures and personality changes characteristic of frontal lobe compression. One of us (J. C. W.) has operated, with temporary success, upon a very similar tumour, which extended forward beneath a post-fixed optic chiasm and thereby brought about severe headaches, personality changes, and epileptiform seizures. This patient showed bitemporal field defects and extensive erosion of the sella

FIG. 2. Extension of a pituitary adenoma upwards between the frontal lobes. Case reported by Müller.[10] (Originally published in *Virchows Archiv.*)

turcica. The cerebrospinal fluid pressure was within normal limits, but the protein content was elevated to 90 mm. per cent. Ventriculogram revealed a filling defect at the base of the third ventricle which extended nearly to the interventricular foramina. On transfrontal exposure the tumour was seen expanding upwards in front of the optic chiasm. After section of the right optic nerve it was possible to remove the greater part of the tumour and much of its capsule. There was immediate relief of the epileptiform seizures with a striking improvement in the patient's mental condition, but this was of short duration. A year later he was hospitalized in a state institution with recurrent convulsive attacks and abnormal behaviour. Removal of this tumour was undoubtedly incomplete, and a further expansion has taken place. Without post-mortem examination no exact knowledge of the

anatomical relationships of this frontally extending adenoma is available, and it therefore does not deserve to be reported at greater length.

We wish to report the following case history of a chromophobe adenoma in detail because of its unusual size and because the post-mortem examination illustrates the two rarest routes of expansion that may take place when a tumour of this type is neglected.

CASE REPORT

William J., a 46-year-old retired chief gunner's mate, began having difficulty with vision in the spring of 1935. He was retired from active service in the U. S. Navy in the same year, but continued to live in China.* In 1938 he first became conscious of restriction in his temporal fields of vision. At this time he was also troubled by diplopia on looking straight ahead, and had to close one eye and use magnifying glasses while reading. He also began to wear dark glasses because bright light hurt his eyes. Following the death of his wife in 1941 he returned to the United States to live with his mother. He then suffered from gradually increasing headaches and more serious loss of vision. He complained not only of constriction of his temporal fields, but also of diminishing acuity, so that he hesitated to go out of the house alone. He also experienced nausea on bending over quickly. His mother noticed a distinct personality change. She was distressed to find that her son, who had always been a "good boy," was becoming irritable, profane at times, and had no greater ambition than to sit in his room all day listening to the radio.

The course of this illness was very insidious until the night of April 9, 1944. That evening he had complained of nausea and had not eaten his supper. At one-thirty a.m. his mother heard an unusual sound in his room and found him having a convulsion. In a little while he recovered and remembered nothing about it, but at seven a.m. he had a second. This was witnessed by the local doctor, who reported "spastic paralysis, twitching, incontinence, and sonorous breathing." He recovered from this seizure, but after a third around noon remained in coma, for which he was sent to the U. S. Naval Hospital in Newport.

On admission at six-thirty that evening he was still unconscious. He had wet himself and bitten his tongue in three places. Examination by Lieutenant Commander Hannibal Hamlin (MC) U.S.N.R., showed a semi-comatose patient with essentially normal fundi and neurological findings. He was given barbiturates and remained stuporous and irrational until the morning of April 12. He then became clear mentally and had no further seizures. Lieutenant Commander Hamlin and the Red Cross worker in Newport were able to obtain a very complete family and past history from the patient and his mother. There was no familial history of epilepsy. The patient's past history was not significant. He had never been interested in girls, but married in 1935. There were no children. During the life of his wife he was not impotent, but apparently had reduced sexual desire and never had any sexual experiences after her death in 1941.

On May 2, 1944, the patient was transferred to the Naval Hospital in Chelsea. To avoid unnecessary repetition, the neurological and laboratory findings at the two Naval Hospitals are given together.

Physical and Laboratory Examinations. The patient was 5 ft., 6 in. tall, of medium weight, and of somewhat feminine build. The penis and testicles were smaller than normal, axillary and pubic hair rather sparse, and he needed to shave only every third day. After recovering

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* Through the kindness of the Bureau of Medicine and Surgery of the U. S. Navy we have been able to obtain copies of the patient's service health record. This states that vision began to fail in the right eye in April, 1935, and by September was reduced to 10/200. The vision in the left eye was still 20/20. No examination of visual fields was made at that time. The diagnosis was optic neuritis of unknown origin. In December, 1939, however, examination at the Regimental Hospital of the U. S. Marines in Shanghai showed definite bitemporal field defects with atrophy of the nerve heads.

from his seizures, he was at first rather belligerent and profane, but gradually became quite cooperative. His mental reactions did not appear definitely abnormal, but he lacked ambition and seemed to have little insight into his condition. Cerebellar tests were performed normally. The cranial nerves, with the exception of the visual tests, were also normal. His ocular movements and pupillary reactions were in no wise impaired. It is important to stress that ordinary tests for smell brought out no diminution in olfaction, which, although surprising, is in line with Jefferson's[9] findings in two out of his three cases. The superficial and deep reflexes, plantar responses, and tests of motor-sensory activity were all within normal limits. Examination and careful questioning of the patient yielded no symptoms or signs suggestive of autonomic disturbances or emotional changes, which have been reported as occurring from compression of the diencephalic centres (Penfield[11]; Bailey[3]; Alpers[1]; Zimmerman[18]).

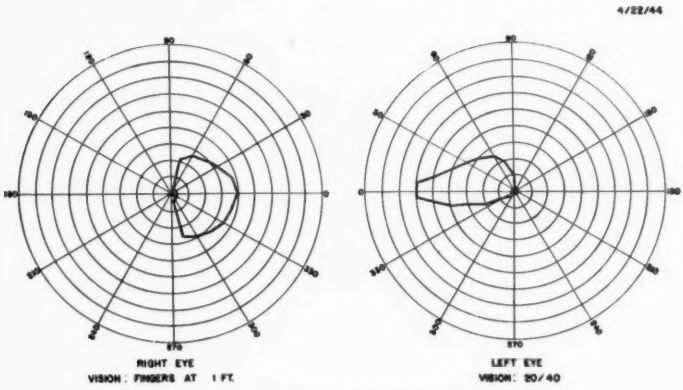

FIG. 3. Visual fields of case reported in text.

Repeated visual examinations showed that his acuity was distinctly reduced: O.D.: Fingers at 1 ft.; O.S.: 20/40. There was a bitemporal hemianopsia with sparing of the macula in the left eye, but not in the right (Fig. 3). The optic discs were slightly pale, but there was no suggestion of papilloedema. The pupils reacted normally to accommodation, but reacted to light only when the beam was projected against the temporal half of the retina (Wernicke's hemianopic pupillary reflex). Action of the external muscles was normal, and there was no limitation of eye movements. There was no engorgement of the superficial veins about the eyes or nose.

X-ray films of the skull disclosed a very large expanding intrasellar neoplasm (Fig. 4). The anterior clinoids were lengthened and tipped upwards and the posterior clinoids greatly thinned and pressed backwards. In addition there was destruction of the dorsum and floor of the sella turcica with erosion into the sphenoid sinus. The pineal body lay in the midline, but was slightly posterior to its normal position.

Lumbar puncture gave an initial pressure of 120 mm. with no cells and a total protein of 53.3 mg. per cent in the spinal fluid.

The electroencephalogram disclosed an abnormal wave pattern. It showed a tendency to moderate slow activity (about 7.5 per second) with marked slow-wave dysrhythmia in the frontal regions. The slow-wave activity in the frontal region was a little more marked on the right than on the left. The moderate slow activity was the same in the parietal and occipital regions, so that there was a definite contrast between these regions and the frontal regions.

The patient's fluid intake and urinary output were within normal limits. Routine blood and urine tests were also normal. The Kahn reaction was negative. The patient's glucose tolerance was within normal limits. Basal metabolism was −15 per cent.

Operations. A diagnosis was made of chromophobe pituitary adenoma with extensive extrasellar extension. Exploratory right frontal craniotomy was carried out on May 9, 1944, through a coronal incision of the scalp. The brain was abnormally tense, but after tapping the anterior horn of the lateral ventricle the frontal lobe was elevated and the floor of the anterior fossa visualized on the right side. The central portion in the region of the olfactory grooves was filled by a well-encapsulated reddish tumour, which extended from the sella turcica between the anterior clinoids and projected forward along the floor of the anterior fossa to the crista galli. The optic chiasm could not be exposed, but the right optic nerve was seen to be greatly compressed by tumour tissue on its medial side. The right olfactory nerve was humped over the dome of the tumour, which expanded upwards at least 3 cm. beneath

FIG. 4. Lateral x-ray of skull to show enormous ballooning of sella turcica with extreme thinning and posterior displacement of posterior clinoids, as well as destruction of floor of sella and erosion forward between the anterior clinoids. The latter are also pressed upwards.

the frontal lobe. Whether this was an olfactory groove meningioma growing posteriorly into the sella, or an unusual anterior extension of a pituitary adenoma, was not at first clear. The gross appearance of the tumour suggested the first possibility; the ballooned-out expansion of the sella seen in the x-ray and the upward displacement of the olfactory nerves were in favour of the second. A biopsy was taken and a generous flap of frontal bone cut on the left side to permit a secondary trans-midline exposure, with either resection of the right frontal pole or a midline exposure of the tumour from above by separating the frontal lobes. The incision was then closed.

The patient made a very smooth recovery, marred by the opening of a small sinus over a buried silk suture, which required over a month to heal. Microscopical examination established the diagnosis of chromophobe adenoma.

The second-stage attack on the tumour was undertaken on July 12, 1944, under intratracheal ether anaesthesia. The previous coronal scalp incision was reopened and the right-sided bone flap turned down. Next the bone on the left was removed, and the bridges across the longitudinal sinus rongeured away. By cutting and elevating the dura right up to the longitudinal sinus and dividing the anterior bridging veins, it was possible to elevate the right

frontal lobe more freely than before. When the tumour was exposed anteriorly, it proved to be much larger than supposed on the previous inspection. It extended posteriorly from the crista galli to a point well behind the right anterior clinoid and far laterally over the lesser wing of the sphenoid. After resecting the tip of the right frontal lobe to obtain a better exposure, we began to scallop out tumour tissue with the electro-cautery loop. This worked nicely and there was at first little bleeding. The compressed right optic nerve was cleared at its origin and tumour tissue removed from the olfactory groove and crista galli on the right side, but it proved impossible to develop the chiasm or the left optic nerve. Although the

FIG. 5. Undersurface of brain with tumour outlined by white dotted line.

patient did not lose any unusual amount of blood, and in spite of transfusion, his blood pressure fell to 50/?. Satisfactory haemostasis was secured by placing small patties of fibrin foam wet with thrombin solution over the tumour bed. When the blood pressure failed to recover, the bone flaps were replaced and the incision closed.

Course. During the evening the blood pressure rose to 110/70, the pulse fell to 100, and respirations to 20, but the patient did not recover consciousness. The vital signs remained satisfactory until six a.m., when there was a sudden change in colour and fall in blood pressure. Death occurred at six-forty-five.

Post-mortem Examination. This was performed eight hours after death by Lieutenant Commander John L. Tullis (MC) U.S.N., and one of us (S. W.). Examination was restricted to the head. Externally, the body was essentially normal. The scalp was shaved, and a clean, sutured surgical incision ran from above and anterior to each ear over the vertex. A large bilateral frontal bone flap was exposed on opening the incision, and beneath this was a slight amount of fresh epidural and subdural haemorrhage.

The frontal lobes were displaced upward by a firm, bulging mass arising from the sella turcica. The anterior and posterior clinoid processes were flattened. The tumour ballooned

out in all directions, compressing and depressing the temporal lobes, bulging between the hemispheres, and extending into the left orbit. The brain and tumour together weighed 1590 grams, the tumour by itself about 150 grams. The roof of the ethmoid and sphenoid sinuses was extremely thin, but not invaded. The tumour was firm, smooth in contour, and slightly granular.

After formalin fixation further inspection of the tumour was carried out. Posteriorly the undersurface presented a mass of firm, white, coarsely nodular tissue covered with a filmy translucent membrane. This extended posteriorly to the anterior margin of the left cerebellar peduncle and to the right anterior border of the pons. It communicated anteriorly with a larger nodular mass showing dark haemorrhagic foci. The total mass extended 9.7 cm. antero-posteriorly and 6 cm. laterally (Fig. 5). As 2 cm. of the anterior pole in the region of the

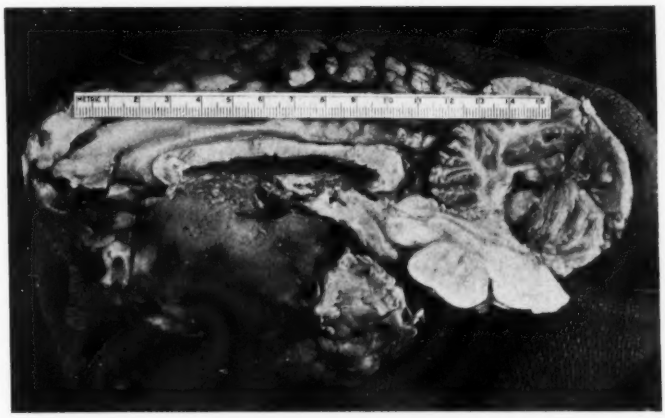

FIG. 6. Sagittal midline section of brain. The anterior, darker portion of the tumour formed the floor of the right lateral ventricle. The posterior, lighter portion extended downwards beneath the brain stem to the pons.

crista galli had been removed at operation, the original over-all length of the tumour was nearly 12 cm. Both temporal lobes were in contact with the mass but were not adherent. Both frontal lobes were molded outward from the midline to accommodate the tumour. On the left the meninges were intact, but displaced; on the right previous surgical removal of the mesial portion of the frontal lobe had exposed the tumour. This region of the tumour presented a raw gray to black granular surface in contrast to the smooth surfaces elsewhere. The left frontal lobe at the point of greatest lateral extent of the tumour was 3.5 cm. thick, while the right at a similar point measured 1.8 cm.

On elevating the tumour posteriorly, the posterior portion of the circle of Willis was clearly seen and was normal, aside from some atrophy of the communicating branches. Both carotid arteries and their cerebral branches were uninvolved, passing lateral to the tumour mass. The right anterior communicating artery entered the tumour mass; the left was free.

The left optic nerve was greatly thinned and so stretched that it could be followed 3.5 cm. forward over the superior and lateral aspect of the tumour. The right optic nerve could be identified at its origin from the brain, but disappeared into a semi-necrotic portion of the tumour, to reappear at the anterior border of the tumour 5.2 cm. anteriorly. Its fibres could not be distinguished in the tumour. The optic chiasm was lost in the tumour.

The left olfactory lobe was thinned, elongated, and stretched 5.3 cm. along the superior lateral margin of the tumour. The right olfactory lobe was similar, measuring 3.8 cm.

On sagittal section the surgical defect in the right lower frontal lobe was clearly visible. A well-demarcated tumour mass rose from the floor of the anterior fossa to a height of 5.3 cm. (Fig. 6). Its upper surface formed a granular floor 3.5 cm. in diameter to the right lateral ventricle and a portion of the third ventricle. The hypothalamus was displaced superiorly and posteriorly, with marked concavity. The left lateral ventricle was compressed but not invaded. The basal ganglia on the left were displaced upward.

Microscopical examination revealed a tumour made up of uniform compact cells with but little stroma. Foci of necrosis and haemorrhage were present. The cytoplasm of the cells was scanty and neutrophilic. The nuclei were regular and occupied up to one-half or two-thirds of the cells. The chromatin was evenly scattered in fine mass. Mitoses were not present. Rare eosinophilic cells were scattered among the chromophobe cells.

Anatomic diagnosis was as follows: Chromophobe adenoma of hypophysis, with compression of hypothalamus, cerebral hemispheres, olfactory lobes, optic nerves, clinoid processes, and right anterior communicating artery; also invasion of right lateral ventricle and optic chiasm.

DISCUSSION

Although the tumour in our patient was much larger than in the cases reported by Jefferson,[9] many of the symptoms and signs produced by it were very similar. The irritability, distaste for company, and loss of ambition, as well as the extreme loss of vision and central scotoma in the right eye, in the presence of normal cerebrospinal fluid pressure but elevated protein, are all similar to Case 2 from the Manchester Royal Infirmary. Jefferson points out that central scotoma and elevation of the protein content of the cerebrospinal fluid are indications of unusual extension of a pituitary tumour.* The wide extension of this tumour and its inclusion of the optic chiasm with a portion of the right optic nerve, as well as the right anterior cerebral artery, made it inoperable. The unusual fall in blood pressure, which occurred at an early stage of the final operation before any undue amount of blood had been lost, was undoubtedly due to disturbance of the contiguous autonomic centres in the walls of the third ventricle. Operative manipulation in the region of the anterior commissure and just posterior to it commonly results in profound changes in pulse rate, blood pressure, level of consciousness, and other vital signs (Dott,[5] White[16]). On thinking back over this case, it would certainly have been wiser to have performed a preliminary ventriculogram. Jefferson[9] has advocated this procedure in all cases in which there is anxiety as to the size of the tumour, and we shall insist on its use in all future cases in which an unusual extension of a pituitary tumour is suspected. Such was obviously the case here, in view of the severe generalized epileptic seizures. In addition, we should have suspected frontal lobe compression had we received in time the social worker's report of the patient's personality changes, which was obtained from his mother. However, even if air studies had been made, the fear of total blindness would have made

* Bilateral central scotomata signify a large retro-chiasmal expansion, since the macular fibres appear to decussate in the posterior part of the chiasma (Henderson[8]). A unilateral scotoma is caused by abnormal localized herniation of the adenoma impinging on an optic nerve (Jefferson[9]).

operation very difficult to refuse. A preliminary ventriculogram, however, would have disclosed the extreme compression of the third ventricle and served as a warning to institute temporary catheter drainage of the lateral ventricles as a post-operative safeguard. This step might have prevented fatal cerebral compression from the wave of oedema which so often follows partial removal of such a large tumour.

If Jefferson's[9] valuable paper had come to hand before this patient's operation, we should have realized from his greater experience that the best solution was to leave such a large growth respectfully alone. In it Jefferson stated that in most cases of pituitary tumours with unusual extensions operation is a course of doubtful wisdom. While his mortality was only 2 per cent for the usual small adenoma, 4 out of 12 patients with extrasellar extensions died.* Finally, operation on long-standing massive tumours is not often profitable for the patient, "as the severe changes in the chiasma brought about by prolonged and increasing compression are irremediable." When confronted by an unusual tumour of this sort in the future we shall first attempt to estimate its size by pneumography. When discretion is judged the better part of valour, radiation therapy can be pushed to the limit, although the chances of a satisfactory response in such widely extending adenomas composed of chromophobe cells are not very bright (Sosman[12]). With continued growth progressive blindness may be unavoidable, but surgical intervention will not become imperative before the advent of obstructive hydrocephalus. Ventricular drainage by catheter passed beneath the scalp from the posterior horn of a lateral ventricle to the cisterna magna, as described by Torkildsen,[13] can then be used as a palliative procedure. After this operation White and Michelsen[17] have found that patients with inoperable brain-stem tumours may live in relative comfort for a period of months to years, until direct compression of vital centres ultimately results in death.

A final point which deserves comment is that the cells of this enormous tumour, which had grown around the optic chiasm and the right anterior communicating artery, showed no evidence of malignancy. Jefferson[9] has pointed out that neither size nor unusual extension are proofs of malignancy, which can only be diagnosed when the pituitary tumour has broken through its capsule and actually invades the surrounding structures. This is the case with the adenomata that invade the cavernous sinus and Meckel's cave, or cause extensive erosion of the cranial base with extension into the nasopharynx, as in the case reported by Bailey and Cutler.[2] In our patient the capsule of the tumour was everywhere intact, and the damage to surrounding structures was caused by simple compression.

* All three of Jefferson's patients with frontal extension survived the operation and appear to have done well, so we do not intend to draw the conclusion that operation should be withheld in all cases when this diagnosis is made. Actually the resection of a small frontally expanding adenoma is liable to be less difficult than that of the more common examples of temporal lobe or hypothalamic extension, particularly if a maximum exposure is ensured by partial resection of the frontal lobe.

SUMMARY AND CONCLUSIONS

1. This article reviews the common pathways of extension of chromophobe adenomas of the pituitary. Aside from the very common invasion of the sphenoid sinus, which causes no injury to the brain or cranial nerves, these include extension upwards into the third ventricle, laterally into the temporal lobe, or into the cavernous sinus.

2. In the two rarest types of extension the tumour may expand down through the incisura of the tentorium to compress the peduncles, pons, and the cranial nerves that arise from this region; or it may work its way upwards into the anterior fossa of the skull, with compression of the frontal lobes.

3. The history of a case is given in detail that illustrates both of these rare types of expansion. During the tumor's ten-year growth it attained a weight of over 150 grams and a length of nearly 12 cm., extending from the crista galli beneath the brain stem to the pons.

4. It produced the classical evidence of compression of the optic chiasm, with nearly total loss of vision in the right eye. In addition, there were clear-cut signs of cortical irritation (generalized epileptiform seizures) and frontal lobe involvement. In spite of its great size and nearly complete compression of the third ventricle, the intracranial pressure remained within normal limits, but the protein content of the cerebrospinal fluid was elevated to 53.3 mg. per cent.

5. At operation the extent of the tumour and its inclusion of vital structures made its removal impossible. Death followed from compression of the autonomic centres in the brain stem.

6. Post-mortem examination showed a chromophobe adenoma of unusual size and extension, with compression of the hypothalamus, cerebral hemispheres, olfactory lobes, optic nerves, and right anterior communicating artery, and with invasion of the lateral ventricle and optic chiasm.

7. In planning operative intervention on hypophysial tumours with signs that suggest compression of structures beyond the optic chiasm, the surgeon should bear in mind the possible pathways of extension that may be followed by slowly growing tumours after rupture of the diaphragma sellae or invasion of the cavernous sinus. Successful surgical removal of the growth under such circumstances is likely to be extremely hazardous and often impossible. A preliminary ventriculogram should facilitate the exposure and aid in determining the operability of such a growth.

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DEPRESSED FRACTURES OF THE SKULL
THEIR SURGERY, SEQUELAE AND DISABILITY

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IN A SERIES of fifteen hundred cases of head injury under observation over a period of time varying from one to fourteen years, 111 were depressed fractures of the skull. Certain principles, based upon the experimental work of Naffziger and Glaser,[18] were followed in their treatment. The purposes of this paper are: (1) to ascertain the final outcome of this type of treatment with relation to the sequelae, and (2) to analyze the cases as to the effects of the injury.

The problem of treatment of depressed fractures consists specifically of: (1) the advisability of elevating the depressed fracture (Fig. 1); (2) the restoration of the cranial defect (Figs. 2, 3 and 4); and (3) prevention of infection.[2,3,8,12,13,14,15,16,17]

With the results of the above-mentioned experiments in mind, it was decided to adopt the following principles in the treatment of clinical cases of depressed skull fractures:

1. To avoid elevation of simple and compound, rounded non-spiculated depressions confined to silent areas of the brain.

2. To avoid elevation of simple and compound fractures in which a large segment of bone was separated, but hinged at one side, and in which, as is usual in fractures of this type, the depth of the depression was not great, if not situated over the motor area.

3. To elevate simple and compound rounded depressions over the motor area.

4. To elevate the fragment in all cases of spiculated fractures.

5. To elevate in all cases where uncertainty existed as to whether spiculation was present.

RESULTS

The results in the series of 111 patients treated may be divided as follows: (1) Complete recovery, 45 patients (40.5 per cent); (2) Partial permanent disability, 30 patients (27.0 per cent); (3) Total permanent disability, 22 patients (19.8 per cent); (4) Fatality, 14 patients (12.6 per cent). A permanent disability was considered present when either the subjective complaints or the objective neurological findings persisted over a period of five years. These people were classified as partially disabled when they were unable to assume a complete return to their former occupations, but could carry out modified work. They were considered totally disabled when they were unable to perform any wage-earning activity.

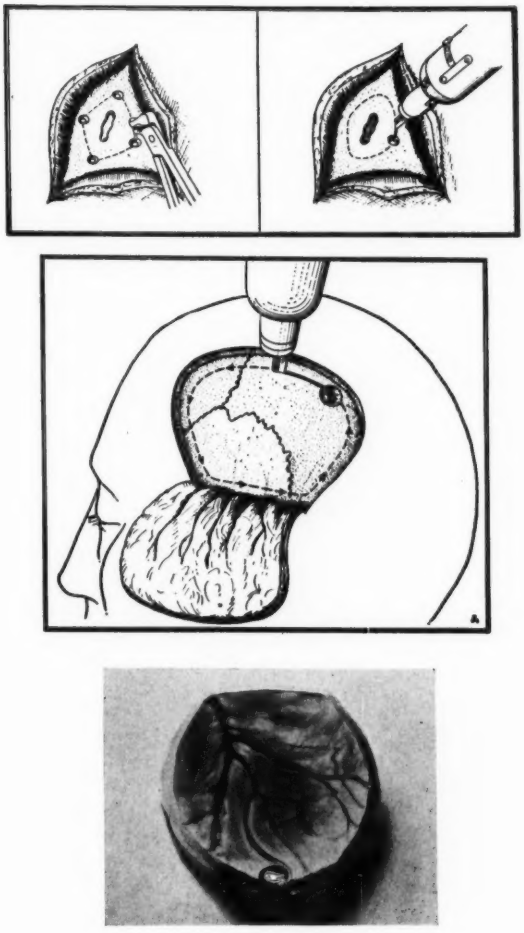

FIG. 1. If one decides to perform a block dissection, the rotary precision cranial saw described elsewhere[8] facilitates the speed and ease of the surgery.

The ages of the patients in the entire series may be noted in Chart I.

COMPLETE RECOVERY

Of these 45 patients, 12 (26.7 per cent) were not rendered unconscious (Chart II). Denny-Brown and Russell[6] have pointed out that in cases of a small area of impact with penetration of the skull cerebral concussion will not take place, even though local contusion or laceration of the brain occurs. In penetrating the skull the force of acceleration is much reduced and the small area of impact focalizes the effects of the injury. These clinical cases

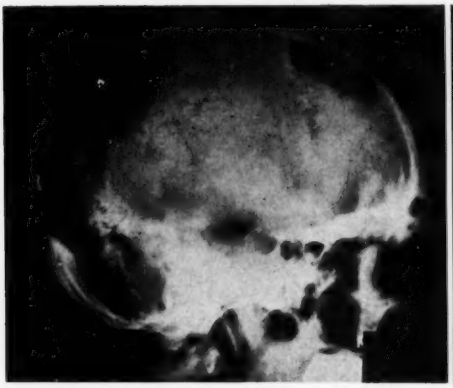

FIG. 2 (*left*). Seven months after an osteo-periosteal graft has been applied. Note the beginning ossification. The surface is firm to palpation. Tantalum is replacing this type of graft.

FIG. 3 (*right*). Three years later. The entire defect shows new bone formation. The edges show marked proliferation with an outgrowth toward the center.

bear out this investigation. In 10 (22.2 per cent) unconsciousness lasted only momentarily; in 18 (40.0 per cent) the patient was unconscious for five minutes to twelve hours, in 1 of these cases (2.2 per cent) the unconscious period being twelve hours. In 4 (8.9 per cent) the unconsciousness was from two to seven days; and in one case (2.2 per cent) eight days. It is noteworthy that 48.9 per cent, or practically half of the group, suffered either momentary unconsciousness or none, while only 5 patients (11.1 per cent) were unconscious two days or longer; 88.9 per cent of the complete recovery group were unconscious less than two days.

FIG. 4. The graft has successfully eliminated the cranial defect (see Figs. 2 and 3).

Of the 45 cases (Chart III), in 18 (40 per cent) the fracture was in the prefrontal area; in 14 (31.1 per cent) it was in the parietal area; in 5 (11.1 per cent) in the temporal region of the skull; and in 8 (17.7 per cent) in the occipital region. In almost one-half of them the fracture was in the frontal area. Consequently, the location of the fracture is a factor in the recovery of the pa-

tient. Of these 45 patients (Chart IV), 28 (62.2 per cent) were operated upon and 17 (37.8 per cent) had no operation.

In regard to the depth of the fracture in the 28 patients that were operated upon (Chart V) 16 (57.1 per cent) were fractures wherein the dura was not penetrated; 1 (3.5 per cent) was subdural; and 11 (39.2 per cent) were intracerebral. In the majority of these cases of complete recovery, the brain was not penetrated, yet patients may recover completely even if such penetration has taken place.

Based upon the experimental work, surgery was avoided in certain instances. The effects of this conservative treatment may be noted (Chart IV). Forty-five patients (40.5 per cent of the entire series) completely recovered. Of these 45, 28 (62.2 per cent) were operated upon and 17 (37.8 per cent) had no operation. These 17 not operated upon represented a group of depressed fractures wherein recovery occurred without any type of surgery

FIG. 5. An extensive flap-like depressed fracture involving the parietal, temporal and frontal bones, without any definite evidence of spiculation: was not elevated: the patient returned to work in 4 months and has been symptom-free for 9 years.

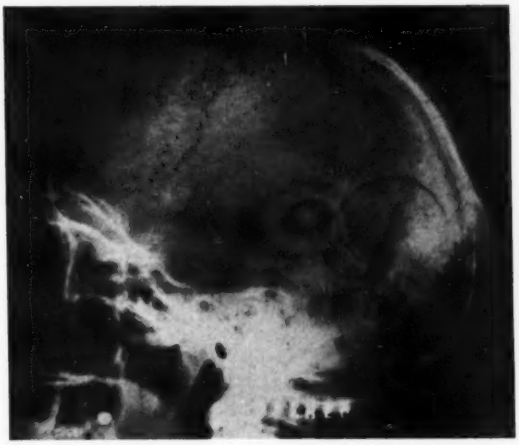

FIG. 6. Depressed area in occipital region: was not elevated: patient symptom-free for 6 years.

whatsoever. Of the 17 not operated upon, 16 had depressions of a simple, rounded type over non-functioning areas of the brain, and consequently we did not deem surgery advisable (Figs. 5 and 6). The seventeenth patient had a spiculated, fragmented depressed fracture situated in the temporal region, which upon x-ray examination appeared as if it penetrated the dura. This fracture was not compounded and because of the severe associated injuries surgery was postponed. When the patient's condition warranted surgical intervention, he was entirely symptom-free and again surgery was postponed. He was observed from time to time over a period of five years and never developed any symptoms referable to his head. About five and a half years after injury he died suddenly of a coronary thrombosis. We thus may conclude that in cases of simple rounded depressions over non-functioning areas of the brain surgery is unnecessary, as indicated by the complete recovery of these patients. Incidentally, fractures of greater severity can recover completely without elevation, though we do not advise the latter as a routine procedure.

PARTIAL PERMANENT DISABILITY

In the partial permanent disability group there were 30 patients (Chart II) of whom 2 (6.7 per cent) were not rendered unconscious. Momentary unconsciousness occurred in 1 (3.3 per cent); unconsciousness lasting 5 minutes to twelve hours in 16 (53.3 per cent); unconsciousness for two to seven days in 3 (10 per cent); unconsciousness over seven days in 8 (26.7 per cent). It may be noted that three of these were either not rendered unconscious at all, or else only momentarily so, and yet a permanent disability occurred. All three patients received sharp localized blows over the motor area which ruptured the dura and caused injury to the underlying brain. One had a hemiparesis and the other two developed convulsions. The majority of this Partial Permanent Disability group were unconscious five minutes to twelve hours, and half of this majority one hour or less.

In this group of 30 (Chart III), 4 (13.3 per cent) sustained the fractures in the prefrontal area; 5 (16.6 per cent) over the motor area; 16 (53.3 per cent) in the parietal area; 3 (10 per cent) in the temporal region; and 2 (6.6 per cent) in the occipital region. In some of this group the motor area was involved, a condition not present in the recovery cases.

Of the 30 patients (Chart IV), 25 (83.3 per cent) were operated upon and 5 (16.7 per cent) were not. Consequently we could accurately determine the depth of fracture in only 25 of the group (Chart V). In 7 of these 25 (28 per cent) the dura was not injured. In one (4 per cent) the dura was torn, but the underlying brain was not lacerated; whereas in 17 (68 per cent) intracerebral damage occurred. From these facts, it is quite apparent that when the brain is lacerated there is a greater possibility for permanent disability.

The sequelae (Chart VI) responsible for the partial permanent disability of these 30 patients consisted of the following factors: post-traumatic neurosis[9] 13 patients (43.3 per cent); epilepsy 11 (36.3 per cent); post-con-

cussion syndrome 10 (33.3 per cent); neurological signs 5 (16.6 per cent); and psychosis 4 (13.3 per cent). Referring to Chart VI, it may be noted that in any individual case there may have existed either one or more of these factors. The organic neurological signs consisted of a mild hemiparesis in three instances, one of these patients having, in addition, a slight motor aphasia; the other two had primary optic atrophy with blindness in one eye.

Let us consider whether the failure to operate upon five of these patients could have been in any way responsible for the sequelae that developed (Chart IV). In four of these cases the depression was very slight and consequently the elevation of the fragments would not have prevented the sequelae. Two of the patients had a mild post-concussion syndrome aggravated by a severe neurosis, and the other two a mild psychosis. In the fifth case a very deep depression was present in the left parietal region, but surgery was refused by the patient. His disability was also due to a mild post-concussion syndrome aggravated by a severe neurosis. In our opinion surgery could not have prevented these sequelae which differed in no way from those in patients with disabilities wherein surgery had been performed.

TOTAL PERMANENT DISABILITY

Of the 22 patients in the total permanent disability group (Chart II), 1 (4.5 per cent) had no unconsciousness; 8 (36.4 per cent) were unconscious for five minutes to twelve hours following the injury; 1 had loss of consciousness 14 hours; 6 (27.3 per cent) for two to seven days; and another group of 6 for eight days to six weeks. Over half (54.6 per cent) had an unconscious period lasting two days or longer. Thus a lengthy unconscious period favors a greater disability. In this group of 22 cases (Chart III), 11 (50 per cent) had the fractures in the prefrontal area; 2 (9 per cent) in the motor area, with development of hemiplegia; 5 (22.7 per cent) in the parietal region; 1 (4.5 per cent) in the temporal, and 3 (13.1 per cent) in the occipital area. Nineteen of the 22 patients were operated upon (Chart IV), and hence we have accurate information as to the depth of fracture in only these. Of them (Chart V), 7 (36.8 per cent) were extradural injuries only, while the remaining 12 (63.1 per cent) were intracerebral. As might be anticipated, a wound entering the brain is much more apt to produce total permanent disability than is one that does not penetrate the dura.

The sequelae responsible for total permanent disability consisted of the following factors (Chart VII): psychoses 13 (59 per cent); neurological signs 9 (40.9 per cent); epilepsy 6 (27.2 per cent); post-traumatic neurosis 5 (22.7 per cent); and post-concussion syndrome 2 (9.0 per cent). Referring to Chart VII, it may be noted that in any individual case there may have existed either one or more of these factors.

Neurological signs were present in 9 cases, and also were associated with either one or more objective findings. These neurological signs consisted of: hemiparesis 2 cases; aphasia 2; loss of vision 4; anosmia 3; loss of hearing 2; and facial paralysis 1.

Of these 22 patients, 19 (86.3 per cent) were operated upon, and 3 (13.7

per cent) were not (Chart IV). Let us once again consider these cases wherein surgery was not performed, and determine whether, if surgery had been performed, the permanent disability could have been prevented. More details regarding the 3 patients in this group that were not operated upon are as follows: the first had a birth injury which we observed some 24 years later. This patient had a definite hemiplegia and mental deterioration dating from birth. Epilepsy developed some weeks prior to our observation. Encephalogram showed cerebral atrophy with a ventricular shift to the side of the depression. The depression was moderately deep and rather wide, but at the time of observation the inner table was very smooth. The second patient had a minor depression in the frontal region, with extensive linear fractures of the skull, and considerable brain damage. Bilateral blindness occurred immediately. Later optic atrophy appeared. The third patient also developed an optic nerve atrophy. It is felt surgery could not have helped in any of these cases.

FATAL CASES

In the entire group there were 14 fatal cases (12.6 per cent). All of these cases came to autopsy. Brain damage was present at the site of injury as well as at a distance. The mechanics of this contrecoup type of damage has been described by Courville.[4]

The ages of the patients at the time of injury, by decades with the number of patients in each group, were as follows: 1 to 10 years (1); 10 to 20 years (3); 30 to 40 years (3); 40 to 50 years (3); 50 to 60 years (1); 60 to 70 years (2); and 70 to 80 years (1).

The duration of unconsciousness (Chart II) was five minutes to twelve hours in 3 cases (21.4 per cent); twelve to forty-eight hours in 7 cases (50 per cent); two to seven days in 2 cases (14.3 per cent); seven days to six weeks in 2 cases (14.3 per cent).

The fractures (Chart III) were located in the prefrontal area in 8 cases (57.1 per cent); the motor area in 3 (21.4 per cent); the parietal area in 2 (14.2 per cent); and the temporal area in 1 (7.1 per cent). Of these (Chart V), 8 (57.1 per cent) were extradural, and 6 (42.9 per cent) were intracerebral.

The cause of death in eight of the fourteen was severe brain damage, consisting of contusions, lacerations, and small and large hemorrhages throughout the brain. Five of these eight patients were not operated upon (Chart IV). These eight patients died at varying periods after the injury, which were three hours; twelve hours; fourteen hours; eighteen hours; twenty-four hours; forty-eight hours; five days; and seven days after injury.

Three of the remaining six patients, in addition to severe brain damage, had an associated subdural hematoma. Two of these were operated upon, and the hematoma removed. Of the remaining three, two died of a meningitis fourteen and twenty days after injury respectively. In both of these the fractures involved the accessory nasal sinuses; the depressions were elevated. In one of them a pneumatocephalus was present. The third patient was ren-

dered unconscious and remained so for a few hours. He had a minor depression and there were no objective neurological findings. The second day, while the attending physician was in the room, the patient without apparent cause suddenly died. Autopsy failed to reveal the cause of sudden death.

SEQUELAE

The sequelae of the entire series consisted of the following objective findings and subjective complaints: headaches, 45 cases (40.4 per cent); dizziness, 30 cases (27.0 per cent); nervousness, 28 cases (25.2 per cent); convulsions, 17 (15.3 per cent); psychosis, 17 (15.3 per cent); eighth nerve disturbance in 11 (9.9 per cent); hemiparesis in 10 (9.0 per cent); abnormality of the third, fourth or sixth cranial nerves in 14 (12.6 per cent); aphasia in 7 (6.3 per cent); first cranial nerve in 7 (6.3 per cent); and second cranial nerve in 5 (4.5 per cent).

It is interesting to note that in a group of 1,000 head injuries with and without skull fracture, headaches, dizziness[7] and nervousness (the post-concussion syndrome) were of considerably greater incidence (67 per cent) as opposed to that in cases of depressed fractures reported by Glaser and Shafer (45 per cent)[10] and by Denny-Brown.[5]

There were 17 patients (15.3 per cent) with traumatic psychosis. A careful analysis failed to reveal any noteworthy features other than that the psychosis developed immediately after the injury in all of them, and that cerebral penetrations were present in 66.6 per cent. [In comparing the incidence of psychosis in cases of depressed fractures to that in a general series of head injuries (Glaser and Shafer)[10] the psychoses were present in only 9 per cent of the patients in the latter group.]

There were also 17 patients (15.3 per cent) who had epilepsy: grand mal attacks were present in 11; focal convulsions in 4; and petit mal attacks in 2.

The percentage of patients with generalized convulsions associated with linear fracture and concussion is low (1.8 per cent).[11] In gunshot wounds the incidence is higher (34.0 per cent), epilepsy occurring most often in the first two weeks after injury.[1,15]

Trauma may produce meningocerebral cicatrix with migration of the ventricles toward the lesions, cysts, localized and diffuse cortical atrophy, but rarely hydrocephalus.

Permanent seizures never developed immediately after injury. In two cases the seizures developed two months after injury and were caused by brain abscesses (Figs. 7 and 8). In four patients they developed nine months after injury; one in one year; two in a year and a half; two in two years; one in four years; one in five years; two in seven years; one in seventeen years; and one in twenty-four years. It is apparent that in this series of cases, as well as in the series of generalized head injuries (Glaser and Shafer[10]), convulsive seizures developed at a late period after injury. This is very important from an industrial standpoint. It would appear that a persistent epilepsy developing at an early period after injury could not readily be consid-

ered activated by the injury. It must be remembered that transient seizures may occur immediately or one week after a severe head injury, due to the serious brain damage, but may never recur. This is also of interest when

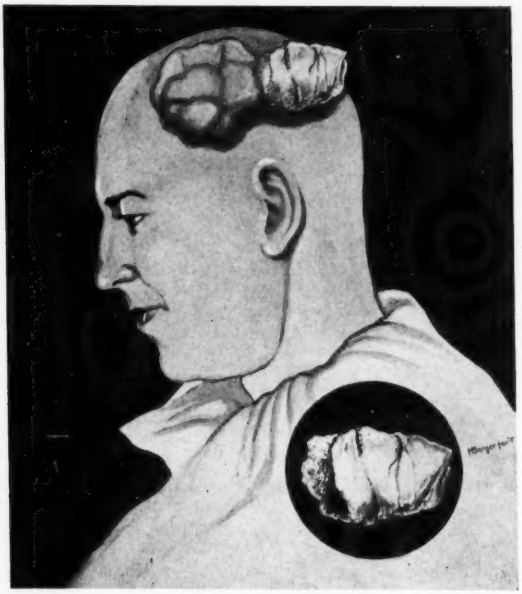

FIG. 7. A brain fungus developed secondary to a brain abscess. The abscess capsule came to the surface and was excised extracranially. Patient developed Jacksonian seizures prior to surgery. He had seizures for 3 years after surgery but has now been symptom-free for 6 years.

FIG. 8. Appearance of patient (see Fig. 7) one year postoperative.

compared to our experimental work, for in these studies a late gliosis developed in from three to nine months after injury.

Unconsciousness occurred in this epileptic group for varying periods.

Three (17.6 per cent) were not unconscious; 6 (35.2 per cent) were rendered unconscious five minutes to twelve hours; 1 (5.8 per cent) twelve to forty-eight hours; 3 (17.6 per cent) two to seven days; and 4 (23.5 per cent) seven days to five weeks. Of the three epileptic patients that were not rendered unconscious, two developed epilepsy from brain abscess; and one was kicked in the head by a horse and the steel shoe penetrated the skull, lacerating the brain.

These fractures were located in varying parts of the brain: 4 (23.5 per cent) involved the prefrontal area; 2 (11.7 per cent) were directly over the motor area; 10 (58.8 per cent) were in the parietal area; and 1 (5.8 per cent) was in the temporal area. None of these fractures primarily involved the occipital lobe. Pathology located in the anterior part of the brain is definitely more prone to give epileptic seizures than that located in the posterior portion. This is not only true of trauma, but of brain tumors.[19]

Surgery was performed in all of the cases, except one. This patient had a depressed fracture at birth and developed seizures twenty-four years after injury. From these facts, it is quite apparent that early surgery is not always instrumental in preventing seizures. It would definitely appear as if the original damage to the brain, or the late formation of adhesions, cysts, etc., are the responsible factors.

The depth of fractures in 3 (18.7 per cent) out of the 16 operated cases was extradural and in 13 (81.2 per cent) intracerebral. Five of these patients with epilepsy had pneumoencephalography performed. In three of the cases there was evidence of ventricular shift to the side of the lesion; a cyst was found in one of these and unequal ventricles were found in the other two.

CHART I

AGE OF ENTIRE SERIES

AGE BY DECADES	CASES	%
1 DAY – 10 YEARS	8	7.2
10 – 20 YEARS	11	10.0
20 – 30 YEARS	37	33.3
30 – 40 YEARS	25	22.5
40 – 50 YEARS	12	10.8
50 – 60 YEARS	13	11.7
60 – 70 YEARS	4	3.6
70 – 80 YEARS	1	0.9
TOTALS	111	100.0

CHART II

UNCONSCIOUS PERIOD

	NO PTS.	NONE		MOMENTARY		5 MIN.-12 HOURS		12 - 48 HOURS		2-7 DAYS		8 DAYS OR MORE		TOTAL
		CASES	%	CASES	%	CASES	%	CASES	%	CASES	%	CASES	%	%
COMPLETE RECOVERY	45	12	26.7	10	22.2	18	40.0			4	8.9	1	2.2	100
PARTIAL PERMANENT DISABILITY	30	2	6.7	1	3.3	16	53.3			3	10.0	8	26.7	100
TOTAL PERMANENT DISABILITY	22	1	4.5			8	36.4	1	4.5	6	27.3	6	27.3	100
MORTALITY	14					3	21.4	7	50.0	2	14.3	2	14.3	100

CHART III

LOCATION OF FRACTURE

	PREFRONTAL		MOTOR		PARIETAL		TEMPORAL		OCCIPITAL	
	CASES	%	CASES	%	CASES	%	CASES	%	CASES	%
COMPLETE RECOVERY	18	40.0			14	31.1	5	11.1	8	17.7
PARTIAL PERMANENT DISABILITY	4	13.3	5	16.6	16	53.3	3	10.0	2	6.6
TOTAL PERMANENT DISABILITY	11	50.0	2	9.0	5	22.7	1	4.5	3	13.1
MORTALITY	8	57.1	3	21.4	2	14.2	1	7.1		
TOTALS	41	36.9	10	9.0	37	33.3	10	9.0	13	11.7

CHART IV

FINAL OUTCOME OF ENTIRE SERIES: RESULTS AFTER SURGERY:

	PATIENTS	%	SURGERY	PATIENTS	%
COMPLETE RECOVERY	45	40.5	OPERATED UPON NOT OPERATED UPON	28 17	62.2 37.8
PARTIAL PERMANENT DISABILITY	30	27.0	OPERATED UPON NOT OPERATED UPON	25 5	83.3 16.7
TOTAL PERMANENT DISABILITY	22	19.8	OPERATED UPON NOT OPERATED UPON	19 3	86.3 13.7
FATAL	14	12.6	OPERATED UPON NOT OPERATED UPON	7 7	50.0 50.0
TOTALS	111			111	

CHART V

DEPTH OF FRACTURE

	EXTRADURAL		LACERATED DURA		INTRACEREBRAL		NOT DETERMINED
	CASES	%	CASES	%	CASES	%	CASES
COMPLETE RECOVERY	16	57.1	1	3.5	11	39.2	17
PARTIAL PERMANENT DISABILITY	7	28.0	1	4.0	17	68.0	5
TOTAL PERMANENT DISABILITY	7	36.8			12	63.1	3
MORTALITY	8	57.1			6	42.9	
TOTALS	38	44.0	2	2.3	46	53.4	25

CHART VI

PARTIAL PERMANENT DISABILITY

TOTAL 30 CASES

CAUSE OF DISABILITY	NO.	%	SURGICAL CASES 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25	NON-SURGICAL CASES 26 27 28 29 30
P. T. N.	13	43.3	■ ■ ■ ■ ■ ■ ■ ■ ■ ■ ■ ■ ■	■ ■
EPILEP.	11	36.3	■ ■	■ ■ ■ ■ ■
P. C. SYN.	10	33.3	■ ■ ■ ■ ■ ■ ■ ■ ■ ■ ■ ■ ■	■ ■
NEUR. S.	5	16.6	■ ■	■ ■ ■ ■ ■
PSYCH.	4	13.3	■ ■	■ ■ ■ ■ ■

EACH NUMBER REPRESENTS AN INDIVIDUAL PATIENT. NOTE THAT MORE THAN ONE CAUSE OF DISABILITY EXISTS IN MANY OF THESE CASES.

CHART VII

TOTAL PERMANENT DISABILITY

TOTAL 22 CASES

CAUSE OF DISABILITY	NO.	%	SURGICAL CASES 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19	NON-SURGICAL CASES 20 21 22
PSYCH.	13	59.0	■ ■ ■ ■ ■ ■ ■ ■ ■ ■ ■ ■ ■ ■ ■ ■ ■ ■ ■	■ ■ ■
NEUR. S.	9	40.9	■ ■ ■ ■ ■ ■ ■ ■ ■ ■ ■ ■ ■ ■ ■ ■ ■ ■ ■	■ ■ ■
EPILEP.	6	27.2	■ ■ ■ ■ ■ ■ ■ ■ ■ ■ ■ ■ ■ ■ ■ ■ ■ ■ ■	■ ■ ■
P. T. N.	5	22.7	■ ■ ■ ■ ■ ■ ■ ■ ■ ■ ■ ■ ■ ■ ■ ■ ■ ■ ■	■ ■ ■
P. C. SYN.	2	9.0	■ ■ ■ ■ ■ ■ ■ ■ ■ ■ ■ ■ ■ ■ ■ ■ ■ ■ ■	■ ■ ■

EACH NUMBER REPRESENTS AN INDIVIDUAL PATIENT. NOTE THAT MORE THAN ONE CAUSE OF DISABILITY EXISTS IN MANY OF THESE CASES.

CONCLUSIONS

1. The following principles should be followed in the treatment of depressed skull fracture: (a) Avoid elevation of simple and compound rounded, non-spiculated depressions confined to silent areas of the brain. (b) Avoid elevation of simple and compound fractures, if not over the motor area, in which a large segment of bone is separated but hinged at one side, and in which, as is usual in fractures of this type, the depth of the depression is not great. (c) Elevate simple and compound rounded depressions over the motor area. (d) Elevate the fragment in all cases of spiculated fractures. (e)

Elevate in all cases where uncertainty exists as to whether spiculation is present.

2. The force of the blow struck, and not the existence of a simple rounded depressed area of bone, is responsible for the underlying brain damage.

3. In those cases wherein extensive brain damage has occurred, early elevation will not prevent sequelae.

4. In this series of 111 cases, complete recovery occurred in 45 patients (40.5 per cent); partial permanent disability in 30 patients (27.0 per cent); total permanent disability in 22 patients (19.8 per cent); fatality in 14 cases (12.6 per cent).

5. If the patient does not return to work within four months, the probability of some type of permanent disability is very great.

6. Approximately 85 per cent of those with momentary or no unconsciousness recovered without disability.

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ELECTROENCEPHALOGRAPHIC STUDIES IN HEAD INJURIES*

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PREVIOUS studies concerning electroencephalographic changes resulting from head injury have for the most part dealt with severely injured patients who were examined days or weeks after the accident. Jasper, Kershman and Elvidge,[7] Glaser and Sjaardema,[3] Williams,[11] and Marmor and Savitsky,[8] whose results have been discussed in a previous report,[2] agreed that there is correlation between electroencephalographic abnormality and severe head injury and that to a degree the clinical recovery of the patient is accompanied by a change of the electroencephalogram from abnormal activity to a more normal pattern. Williams[11] studied a few patients who had sustained mild injuries and observed that normal records might be obtained within a few hours of the injury. We believed that electroencephalographic examination of a large number of patients with mild head injuries a few minutes following injury might be of value in determining the onset and duration of the electroencephalographic changes and might throw some light on the mechanism of concussion.

The work to be reported here was begun in 1942 and a preliminary report was published in 1944.[2] Since this earlier report was submitted for publication, two reports of electroencephalographic studies in head injury patients have appeared. Heppenstall and Hill[6] reported a study of 150 patients suffering from chronic posttraumatic syndromes of which 87 were thought to be on an organic basis and 63 on a functional basis. They found in these chronic cases that the length of time that had elapsed since the head injury bore no relation to the electroencephalographic result. Whether the abnormality of the record was focal or generalized was also studied. The focal abnormalities were found significantly more often in the 87 patients with negative personal histories for previous neurotic or psychiatric disorders who suffered from true postconcussive states, traumatic epilepsy, or had long posttraumatic amnesia, while diffuse abnormalities were more common in the 63 patients who exhibited functional symptoms and short posttraumatic amnesia and who had positive personal histories for previous neuropsychiatric disorders. They suggested that focal abnormalities in the electroencephalogram are more likely to be associated with acquired cerebral trauma and diffuse abnormalities with constitutional deficiencies. These findings are of great interest, but some criticism may arise because the localization of the abnormali-

* The work described in this paper was done under a contract recommended by the Committee on Medical Research, between the Office of Scientific Research and Development and the University of Oregon Medical School.

ties was determined by an electroencephalographic technique in which only four scalp electrodes were applied. A preliminary report on the value of electroencephalograms in the prognosis of minor head injuries has been published by Harris, Wittson and Hunt.[5] This report contains information on only 4 cases. It will be of interest if further work by these authors shows that one can predict by the use of the electroencephalograph which head injury patients may be expected to have prolonged symptoms.

Since our earlier report[2] the work has been continued to include patients with more severe injuries and recheck records have been obtained upon as many patients as possible following recovery. The report presented here is an electroencephalographic study of 213 patients who sustained head injuries at the 3 shipyards operated by the Kaiser Corporation in or near Portland, Oregon.* Records were taken upon 197 patients at the First Aid Station of the Oregon Shipbuilding Corporation. The remainder of the electroencephalograms were obtained on 16 severely injured patients as soon as possible after they had been admitted to local hospitals.

MATERIAL AND METHODS

In the series studied there were 185 men and 28 women. The age range was from 16 to 87 years, the mean age being 36.3 years.

The recording technique has been described (Dow, Ulett and Raaf[2]). Bipolar recording from six electrodes was used. The electrodes were applied by means of a headband electrode holder with six spring contact electrodes (Ulett and Claussen[9]), as illustrated in Fig. 1. With this device it was occasionally possible to start taking a record within ten minutes after the patient had been struck on the head. All but 26 of the 213 patients had records taken within 24 hours of injury and over one-half of the 213 had records taken within an hour of injury. Most of the records upon the more severely injured who were hospitalized were taken within the first 24 hours and a few were taken less than eight hours after the accident. Follow-up records were taken on 86 of the series of 213 patients.

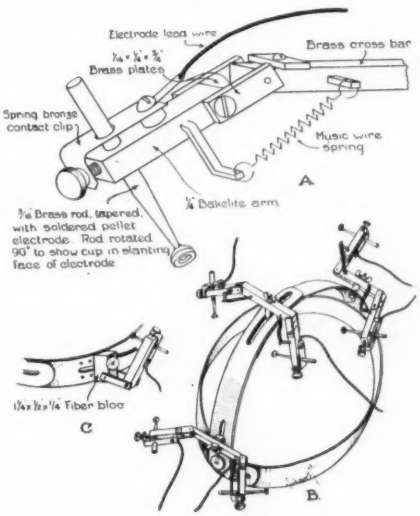

FIG. 1. Headband electrode holder.

A history was elicited when the patient was brought to the First Aid Station or hospital. Opinions of the patient, witnesses of the accident, ambulance men, safety inspectors, and attending physicians were recorded and evaluated in an attempt to obtain an accurate account of the accident. The scene of the accident was visited in almost all instances by one of us (G.U.) and an attempt made to evaluate the physical factors responsible for the injury. When the patient had been struck on the head by a falling object, that object or an identical one was found and

* We are indebted to the Kaiser Company and to the Oregon State Industrial Accident Commission for their excellent cooperation throughout this study.

weighed and the distance of the fall measured. When the patient fell his weight was estimated and the height of his fall measured. In 83 of the cases studied some approximation of the velocity of either the falling object or the person at the moment of impact in foot-seconds was calculated and the force involved in foot-pounds was determined. Other pertinent facts concerning the accident were obtained from an efficient and highly organized staff of safety engineers.

A general examination was performed on all patients immediately after the electroencephalographic record had been taken. The blood pressure, pulse, temperature, and respiration were recorded and all patients were examined for evidence of injury. Of the 213 patients studied, 201 had laceration and/or contusion about the head. Two of the patients had tender painful necks and one had a fracture of the seventh cervical vertebra. Two had x-ray evidence of skull fracture. In only seven patients was there no external evidence of head injury but the history and statements by witnesses that these patients had been struck on the head were so definite they were included in the series. A neurological examination was likewise conducted and the patient's sensorium evaluated. The account of events at the time of the accident as told by the patient enabled us to make some estimate of the period of amnesia during which he was mentally out of contact with his environment. In those cases in which there was impairment of sensibility at the time of examination, the term "unconsciousness" was avoided and the state of the patient's insensibility was graded as (1) coma, (2) semicoma, (3) mild, moderate, or severe confusion. In defining these terms we followed the usage outlined by the Medical Research Council Brain Injuries Committee of Great Britain.*

As a control, records were taken during the course of the study on 211 persons who were considered "normal" subjects. There were 171 men and 40 women in the control series; their age range was 16 to 77 years, the mean age being 34.3 years.

In order to evaluate the factor of old cerebral trauma, both the control subjects and the patients with head injuries were asked whether they had experienced previous head injuries severe enough to have produced definite amnesia. Fifty-eight of the 213 patients in the head injury series and 70 of the 211 persons in the control series gave the history of having had such a blow on the head. In both the injury series and the control series the electroencephalographic records of those who had had a previous injury showed no increase in abnormality as compared with those who had not sustained a previous injury.

To insure uniformity within this study, all records that were taken were graded by the same persons.† The records were classified as "normal," "borderline," or "abnormal." A range of dominant activity from and including eight to twelve cycles per second was considered normal. Slow waves below eight per second were called abnormal. Lack of definite pattern, despite high amplification and bursts of high voltage activity against a normal background, was considered indicative of abnormality. The greater the amount of slow or fast activity in a given record the more the normality of the record was held in question (Fig. 2).

RESULTS

Comparison of the Electroencephalograms of the Head Injury Patients and Controls. When the electroencephalograms on all of the 213 patients in the head injury series were compared with the electroencephalograms on the 211 patients in the control series it was found that 62 per cent of the control patients had normal electroencephalograms whereas 53 per cent of the electroencephalograms on the patients in the head injury series were normal (Fig. 3). Thirty per cent of the control series had borderline records whereas

* Medical Research Council Brain Injuries Committee. *A glossary of psychological terms commonly used in cases of head injury.* London: H. M. Stationery Office, 1941.

† We are indebted to Doctor Knox Finley for his aid in record interpretation.

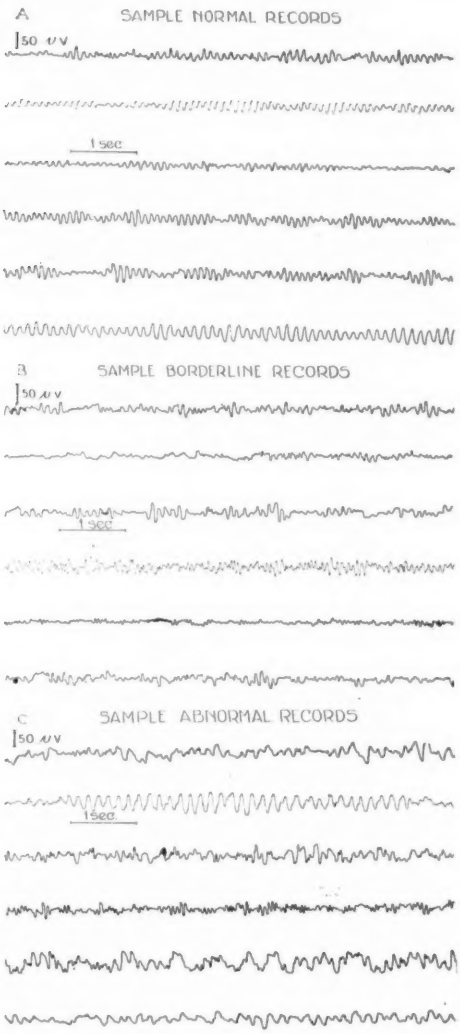

FIG. 2. Examples of (A) normal, (B) borderline, and (C) abnormal electroencephalographic records. There are six cases in each group and each record is from the left parieto-occipital lead.

36 per cent of the head injury patients had this type of record. Distinctly abnormal records were found in 8 per cent of the control series and in 11 per cent of the head injury series. It is thus evident that when the electroencephalograms of the entire group of head injury patients were compared with

the electroencephalograms of the entire control group only slight difference could be detected.

Correlation of Electroencephalographic Findings With Clinical Evidence of Concussion. We divided the head injury patients upon whom we took electroencephalographic records within 24 hours of the injury into groups depending on the severity of symptoms. Out of the total of 187 such patients 31 had no symptoms except pain at the site of injury. No degree of cerebral trauma was thought to have existed in these patients. One hundred patients had complained of symptoms, such as "dazed feeling," "saw stars," dizziness, diffuse headache, or nausea which came on immediately after the in-

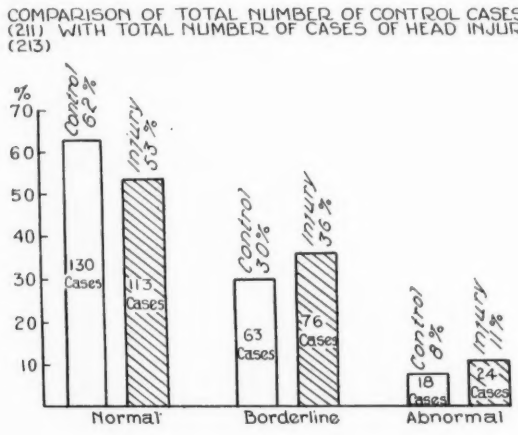

FIG. 3.

jury. There was, however, no definite period of amnesia and no impairment of consciousness at the time the record was taken. We considered patients in this group had suffered cerebral trauma of +1 severity. Forty-six patients gave a definite history of amnesia of some duration as a result of the accident but there was no impairment of consciousness at the time the records were taken. This group was regarded as having suffered cerebral trauma of +2 severity. Ten patients exhibited mild, moderate, or severe confusion at the time the record was taken. They were considered to be more severely injured and were classed as +3. A category of +4 severity was reserved for patients in coma or semicoma. There were no patients in this group in our series (Table I). Fig. 4 shows the percentage of normal, borderline, and abnormal records among the patients suffering from the various degrees of cerebral trauma. It will be noted that the +1 group, which falls short of true concussion as usually defined, deviates very little from the normal control group in the percentage of normal, borderline, and abnormal records. There is a slight but significant shift toward the abnormal in the cases of +2 clinical severity and a decided shift in the +3 category. No patient who

exhibited any degree of impaired consciousness at the time the record was taken had a perfectly normal electroencephalogram and five out of ten were

TABLE I

CLINICAL CLASSIFICATION OF SEVERITY OF CEREBRAL TRAUMA

DEGREE	NO. OF PATIENTS WITH RECORD WITHIN 24 HRS.	SYMPTOMS
0	31	Scalp laceration and/or contusion. No cerebral symptoms.
1+	100	Dazed feeling, dizziness, "saw stars," diffuse headache, nausea, no amnesia for the accident, no impairment of consciousness when E.E.G. was taken
2+	46	Definite amnesia of some duration. No impairment of consciousness when E.E.G. was taken.
3+	10	Mild, moderate or severe confusion when E.E.G. was taken.
4+	0	Coma or semicoma at time that E.E.G. was taken
	Total — 187	

distinctly abnormal. In none of the 10 patients who fell in the +3 group was there any history of a previous head injury with amnesia, or a family or personal history of nervous or mental disease. Although one is perhaps not

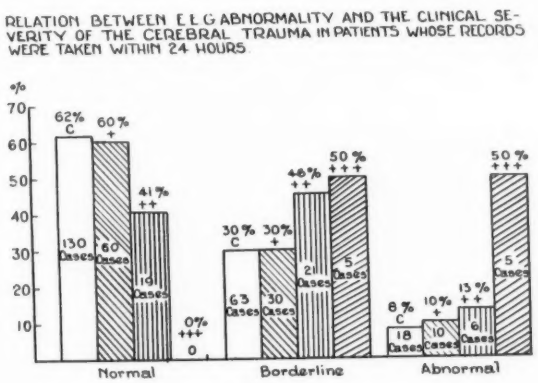

FIG. 4.

justified in expressing in percentage a group of only 10 individuals, it is done here for comparison with the other larger groups. Subsequent electroencephalographic records have been taken on 4 of these 10 patients. Two of these 4 patients subsequently had normal records, in 2 the recheck records were the same as the original, and in 6 no rechecks have been run. The follow-

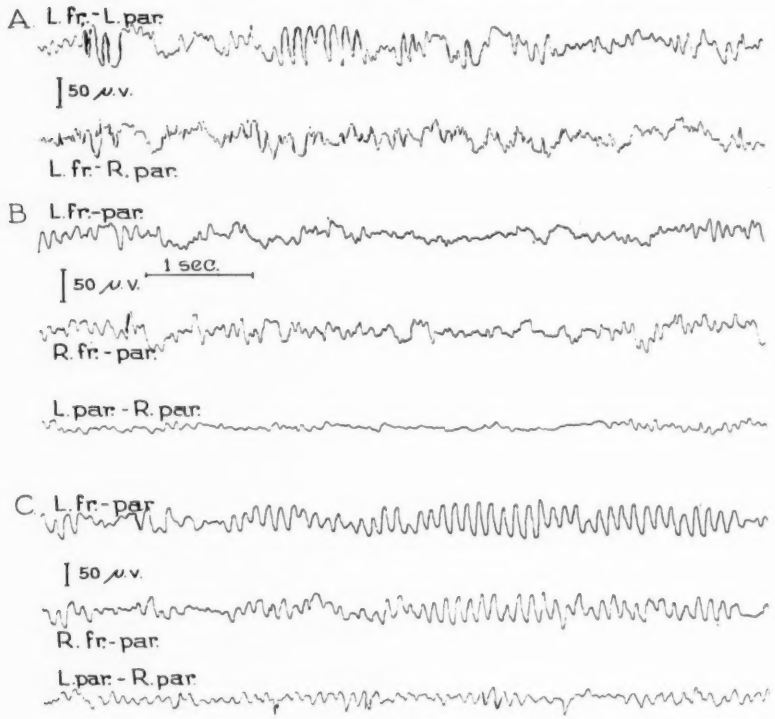

FIG. 5. Electroencephalographic records in Case 61. (A) Record started thirty minutes after trauma. A definitely abnormal pattern. (B) One hour and twenty minutes after trauma. The record was still considered abnormal. (C) Sixteen days after the trauma. The record now was normal.

ing case report regards one of the patients with concussion who at first had an abnormal electroencephalographic record but later displayed a normal tracing.

Case 61. An 18-year-old welder's helper fell about 10 feet striking his head upon a steel deck. A witness said that the patient was "unconscious" for about a minute. In the First Aid Station the patient seemed to be in a state of mild confusion. He had a 2-cm. scalp laceration in the region of the left forehead but there was no evidence of depression in the skull. Examination at the First Aid Station revealed no abnormality in the routine neurological examination. The patient was seen by one of us (J.R.) about 4 hours later. At this time he had no memory of the accident or the events that had occurred at the First Aid Station. His blood pressure was 104/60 and his pulse 80. The neurological examination again revealed no abnormalities except that the right pupil was slightly larger than the left. Roentgenograms of the skull showed no fractures. The clinical diagnosis was cerebral concussion. Fig. 5 illustrates the electroencephalographic findings on this patient at various intervals following head injury. A completely normal record was obtained 16 days after injury.

Time Interval Between Injury and Taking of the Electroencephalogram. If the disturbance in the brain cells in concussion is a reversible process, then it follows that the earlier after the injury one can take the electroencephalographic record the greater the chance of obtaining an abnormal record. We were able to start taking electroencephalographic records on 53 patients within 30 minutes of the time of injury. Seventy-one patients had their electroencephalograms started within 30 to 60 minutes after the accident. Sixty-three records were obtained when the elapsed time was between 1 and 24 hours, the vast majority of these being obtained before 2 hours had elapsed. Records on 26 patients were taken when more than 24 hours had elapsed since injury. It was found that the percentage of distinctly abnormal records was slightly greater in the patients examined within 30 minutes than in patients examined after 30 minutes. Nine out of the 24 patients having abnormal records in the injury series had their records started within 30 minutes of the accident. It would seem, therefore, that if one is to detect a large percentage of abnormalities in the electroencephalograms on patients with mild head injuries, such as those we have studied, one must examine the patients very soon after injury. One patient described in the earlier report[2] exhibited a normal electroencephalographic record within 15 minutes of the time he sustained a true concussion as judged by his clinical symptoms. It is obviously impossible to demonstrate the time of onset of the abnormal waves in cases of human concussion.

Correlation Between Physical Factors in the Blow and Abnormality of Electroencephalographic Records. Many difficulties were encountered in attempting to analyze the physical factors in this series of head injury patients. Steel helmets not only reduced the number of head injuries but also complicated the difficult task of estimating the force of the blow. Another feature which at times hindered mathematical expression of the forces involved in a given accident was the difficulty of determining accurately how far an object fell. The weight of falling objects could usually be determined. Whether the blow was direct or glancing was often impossible to ascertain. When a board of some length fell it was impossible to know whether the full weight struck the patient on the head. The forces involved when the patient fell were even more difficult to determine. The rapidity of movement of the head at the moment of impact might be greater or less than the acceleration of gravity because of muscular movement during the fall.

We have recognized that even under the relatively favorable conditions for studying these patients at the Oregon Shipbuilding Corporation it would hardly seem possible to determine accurately the velocity at impact and the foot-pounds of energy involved. However, in our series there were 78 patients upon whom electroencephalograms were taken within 24 hours of injury and in each of these cases some estimate could be made of the physical factors. In 77 the velocity of either the object striking the patient or the velocity of the patient's head at termination of the fall could be expressed in feet per second. In 74 cases it was possible to arrive at some kind of a fig-

ure for foot-pounds of energy involved in the blow. It is common experience that the greater the force of a blow the greater the damage to the skull and cerebrum. The question whether concussion is related to the force of a blow or to the acceleration or deceleration of the head has been recently investigated by Denny-Brown and Russell,[1] Gurdjian and Webster,[4] Walker, Kollros, and Case.[10] In our series the average velocity at the moment of impact was 24.1 feet per second in the group with normal electroencephalograms, 25.8 in the borderline group, and 34.2 in the abnormal group (Table II). It is of interest that the threshold velocity for concussion at the moment of impact in the cat and monkey, according to Denny-Brown and Russell,[1] is 28 feet per second and this figure is between the average velocity in the

TABLE II

PATIENTS SEEN WITHIN 24 HOURS
COMPARISON BETWEEN ELECTROENCEPHALOGRAPHIC RECORDS AND THE PHYSICAL FACTORS IN THE INJURY

NORMAL 32 cases	24.1 ft sec. Range 8-56	324.2 ft.lb Range 4 - 1650
BORDERLINE 33 cases	25.8 ft sec. Range 8-50	581.0 ft. lb. Range 5 -2400.0
ABNORMAL 13 cases	34.2 ft. sec. Range 8-62	1077.2 ft.lb. Range 5-4500.0

abnormal and borderline electroencephalogram groups in our series. The average foot-pounds of energy in the blows sustained by the patients who had normal electroencephalograms was 324.2. In the group of patients who had borderline records the average foot-pounds of energy was 581.0 and among those with distinctly abnormal records the average was 1077.2. The range within each group was wide but this is expected in view of the difficulties of estimating physical factors in an accident. It is difficult to judge from our data whether it is the force of the blow or the acceleration or deceleration that is responsible for the electroencephalographic changes.

The relationship between the severity of the symptoms and the velocity of the head at the moment of impact or the velocity of the object striking the head at the moment of impact is revealed in Table III. The relationship between severity of the symptoms and the foot-pounds of energy involved has also been tabulated. Among the patients whose symptoms were graded 2+ or 3+ (these groups represent true concussion) the average velocity of the head or of the object that struck the head is well above the threshold necessary to produce concussion as determined experimentally by Denny-Brown and Russell.[1] The average velocity involved in the cases in which the patient's cerebral symptoms were graded zero or 1+ was well below this threshold figure.

Correlation Between Electroencephalographic Findings and the Time the Patient Lost from Work. The patients examined within 24 hours of their injury were divided into two groups on the basis of the amount of time lost

TABLE III

COMPARISON BETWEEN THE CLINICAL SYMPTOMS AND THE PHYSICAL FACTORS IN THE INJURY

CLINICAL SEVERITY OF INJURY	AVERAGE VELOCITY	AVERAGE FT. LB. OF ENERGY
0	(6 cases) 18.4 ft/sec. Range 13-35	(6 cases) 38.6 ft.lb. Range 5-75
+	(44 cases) 21.5 ft/sec. Range 8-56	(42 cases) 321.8 ft. lb. Range 4-2,250
++	(25 cases) 31.2 ft/sec. Range 11-62	(24 cases) 768.1 ft.lb. Range 20-8,400
+++	(6 cases) 31.5 ft/sec. Range 22-50	(6 cases) 1,028.3 ft.lb. Range 720-4,500

from work. Thirty-nine patients required more than 24 hours time off duty because of head injury. Their electroencephalographic records were compared with the records of 148 patients who went back to work within 24

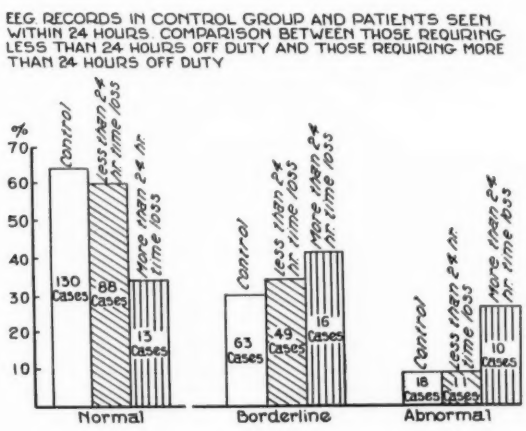

FIG. 6.

hours of injury. Fig. 6 shows the difference in the two groups of records. It can be seen that the records on patients who required less than 24 hours time off did not vary appreciably from the records taken on the controls in respect to the percentage of records that fell into the normal, borderline,

and abnormal classifications. Among the 39 patients who took more than 24 hours off as a result of head injury, 13 had normal records, 16 had borderline and 10 had abnormal records. Therefore 67 per cent of the patients who took more than 24 hours off duty had borderline or abnormal electroencephalographic records. Patients who took more than 24 hours off duty and those who took less than 24 hours off duty were studied from the standpoint of severity of injury as judged by clinical symptoms (Fig. 7). Seventy-three per cent of the patients requiring more than 24 hours off fell in the +2 or +3 grades of clinical severity. This figure approximates the 67 per

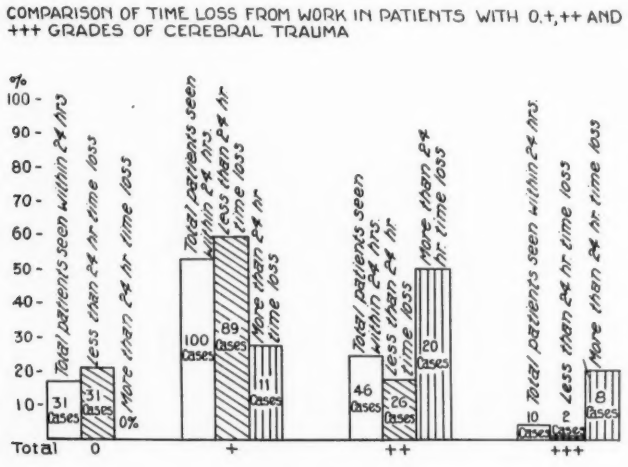

Fig. 7.

cent of the patients who had borderline or "abnormal" electroencephalograms. A study of the patients who required less than 24 hours off duty revealed that the electroencephalographic study is less reliable than the clinical classification of the case in predicting time loss, for only 19 per cent of those requiring less than 24 hours off were in the +2 or +3 groups while 41 per cent of the patients who required less than 24 hours time off fell within the borderline or abnormal electroencephalographic classification. Therefore we believe the value of an electroencephalogram in predicting time loss that will result from a given accident is limited. It must be noted, however, this result may be somewhat colored by the fact that many patients were deterred from returning to work by physicians who, having no access to the interpretation of the electroencephalograms, based their advice entirely on the severity of symptoms.

Analysis of the electroencephalographic changes in 56 patients judged clinically to have had true concussion is shown in Fig. 8. In this group of patients, those with borderline or abnormal electroencephalograms were more

likely to require more than 24 hours time off than those with normal records. Here again the electroencephalogram is of limited value in an individual case, for 54 per cent of the 28 patients who had true concussion and required less than 24 hours off had borderline or abnormal electroencephalographic records.

Follow-up Study of Patients. Recheck records were taken on 86 out of the total of 213 shipyard workers who were examined electroencephalographically following acute head injury. The first electroencephalogram was taken within 24 hours of the time of injury in 81 of these 86 patients and in 6 the electroencephalogram was started within 15 minutes after the trauma. The

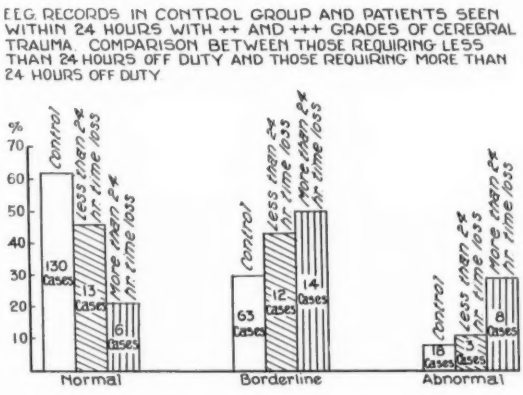

FIG. 8.

average interval between the final electroencephalogram and the accident was 8 weeks.

Sixteen of the 86 patients showed a change in the type of record between the first and last recording. Of five patients who originally had abnormal records, three subsequently had borderline and two subsequently showed normal records. Of 11 patients with borderline records, 10 later had normal records while one patient who originally had a borderline record later had an abnormal record. None of the 34 patients whose original record was normal changed when the record was repeated after clinical recovery. Fig. 9 shows that the 70 head injury patients who did not change after clinical recovery had a percentage of normal, borderline and abnormal records which closely resembled those of the normal control group. It was our conclusion that the electroencephalographic changes produced by head injuries of the severity we were studying are reversible.

It might be expected that one would find a more severe type of head injury among those patients whose electroencephalograms showed a change between the first and second records than among those whose second electroencephalograms were in the same classification as their first and therefore the

electroencephalograms were probably not affected at all by the injury. This view is seemingly supported by the fact that 7 out of the 16 workers in this group were to be found among the 36 injury cases (from the total 213 cases) who required more than 24 hours time loss following the accident. An analysis of the physical factors in the blow indicates that these 16 patients suffered more severe injuries. These patients were struck at an average velocity of 32 feet per second at impact and an average force of 717 foot-pounds. The patients whose recheck record showed no change were struck with an average velocity of 27 feet per second and a force of 556 foot-pounds.

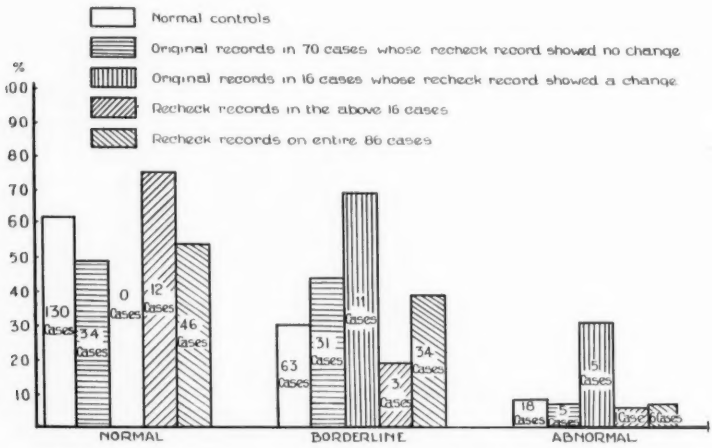

FIG. 9. A comparison between the normal controls, patients whose subsequent record showed no change and those who did subsequently change in respect to the percentage of normal, borderline, and abnormal records in the original and recheck records.

A study regarding the clinical severity of symptoms among the 16 patients whose original electroencephalographic records differed from their second records revealed that there was a greater percentage of these patients that fell in the 2+ and 3+ categories of clinical symptoms than was true of the entire group of 213 patients. However, two patients who clinically were thought to have zero degree of cerebral trauma and 5 who suffered from 1+ degree of cerebral trauma exhibited a shift of electroencephalographic pattern to a more regular pattern upon recheck. Possibly individual differences in the stability in the electroencephalogram may help to explain the wide range in the tables where physical factors were correlated with electroencephalographic abnormality. It is well known that there is great individual variation in the effectiveness of overbreathing, alcohol consumption, and blood-sugar reduction in the production of electroencephalographic abnormality. It is not unlikely that the electroencephalogram following cerebral trauma is likewise influenced by individual differences. Age may be one of the factors responsi-

ble for this instability of the electroencephalogram after mild trauma. The majority of the seven patients who showed a change in their electroencephalograms after 0 and 1+ degrees of cerebral trauma were near the extremes of the age groups in this present series. One patient was 67 and the average age of the remaining 6 was 26 years as compared with 36.3 years for the whole series.

An analysis of the types of change found between the initial and final electroencephalographic records reveals that non-specific phrases such as "better organization" and "fewer irregularities" best characterize the trend

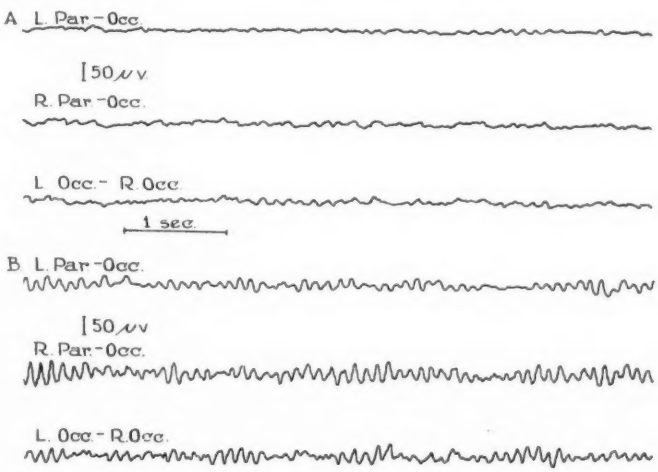

FIG. 10. Electroencephalographic record in Case 117. (A) The record was started forty minutes after trauma. A borderline low voltage pattern. (B) Two months after the trauma. This record was now normal.

toward normalcy seen in the second or final record. In 9 patients marked increase in voltage was seen in the second record. Such a change is illustrated by Case 117.

Case 117. A 30-year-old worker fell backwards. His head travelled approximately 5 feet to strike a steel plate. There was a posttraumatic amnesia of about 15 minutes' duration and a retrograde amnesia of 2 minutes' duration. Neurological examination revealed no abnormalities although the patient was dazed until the time the electroencephalogram was started 40 minutes after the accident. This record showed 6 to 9 per second activity and was almost flat in many places (Fig. 10A). The highest voltage waves were about 15 micro-volts. Two months later the patient was again seen. He had been clinically normal since the day of the accident and had lost no time from work. His amnesia remained unchanged. An electroencephalogram taken at this time showed well organized 9 to 10 per second activity with a voltage of from 40 to 50 micro-volts (Fig. 10B).

In 11 patients the frequency changed from a pattern of abnormally slow waves to one well within the normal range of 8 to 12 per second (Fig. 5). In-

creased frequency and amplitude usually went hand in hand but there were a few exceptions to this.

In 4 cases more than two records were taken. In one of these (Case 61, Fig. 5) the high voltage slow waves seen 30 minutes after trauma were replaced 50 minutes later by waves of lower voltage. A similar though less striking sequence was also seen in another patient who suffered a blow of like severity. The two remaining patients failed to show this sequence.

In view of the highly variable changes that occur and the finding of patterns that did not undergo alteration with clinical improvement in patients, it is not possible to suggest an electroencephalographic pattern that could be said to be characteristic of a given series of pathological changes as the patient returned to normal.

SUMMARY

1. If mild cerebral trauma such as we were investigating produced changes in the electroencephalographic tracing, the abnormality disappeared within a period of minutes in the vast majority of cases.

2. Patients who gave a history of amnesia following cerebral trauma, but were clear mentally at the time the electroencephalogram was taken, showed only a slight increase in the percentage of abnormal records as compared to the control series. This was true even when the records were taken within a few hours of the accident.

3. If there was an impairment of consciousness of any degree at the time the electroencephalogram was taken, abnormality in the electroencephalogram was the rule.

4. Electroencephalographic records that were started within 30 minutes after patients sustained head injury showed a greater percentage of abnormality than those taken after 30 minutes had elapsed. The rapid disappearance of abnormal electroencephalographic findings points, in our opinion, to some mechanism in concussion other than petechial hemorrhage, cerebral contusion, embolic phenomenon, or any other histopathological change which must of necessity require several days to disappear.

5. In the patients with abnormal electroencephalographic records the average velocity of the striking object or of the falling head at the time of impact was greater than the velocity necessary to produce concussion in experimental animals as determined by others. The average velocity of the striking object or falling head in patients who showed normal or borderline electroencephalographic records was less than the velocity necessary to produce concussion in experimental animals.

6. The forces and velocities at impact that appear to be necessary to produce true concussion in humans appear to be of the same order as those found necessary to produce "experimental concussion" in animals.

7. When the 39 patients who required more than 24 hours time off from work were compared with the remainder who required less than 24 hours time off, the former group had a greater percentage of abnormal records and

a more severe injury as judged by their clinical symptoms at the time the record was taken. However, the study of the electroencephalographic records taken immediately following mild head injury was less reliable than clinical judgment in predicting time loss from work.

8. Only 16 patients out of 86 reexamined after clinical recovery showed a change in their record of sufficient degree to change them from one group to the other. Fifteen shifted toward normalcy and one patient showed a shift from the borderline to an abnormal record.

9. The patients showing a change in the records were on the whole a more seriously injured group than the patients who did not show any shift. However, several patients received cerebral trauma which fell short of what is usually considered true concussion and yet exhibited a definite improvement in the electroencephalogram when it was repeated at a considerable period after the accident. This suggests the possibility that there is a different susceptibility to electroencephalographic changes in different individuals following trauma. There was some evidence that age may be a factor in this susceptibility to electroencephalographic instability.

10. An analysis of the wave form, frequency and voltage of the brain activity encountered in the electroencephalograms in patients whose subsequent electroencephalogram showed improvement did not allow the designation of any particular activity that seemed characteristic of the electroencephalogram following mild cerebral trauma.

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"DELAYED RECOVERY" IN PERIPHERAL NERVE LESIONS CAUSED BY HIGH VELOCITY PROJECTILE WOUNDING*

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IN DEALING with a large number of peripheral nerve injuries due to war wounds, we have been impressed with the number of patients who recover function spontaneously, and with the satisfactory degree of recovery that many of them eventually attain. Even in the cases that have been explored with the expectation of finding the nerve trunk completely severed, a surprisingly large percentage have shown no disruption of continuity of the nerve. These observations seem to apply less to the incisional type of wound due to bayonets, knives and the like, but to be more characteristic of the wounds due to high velocity projectiles. In order to confirm our impressions, we have analyzed the histories of 154 men with lesions involving one or more of the three major nerves to the hand, whose wounds were due to projectiles. In 80 cases the wounding agent was a bullet, and in 75 instances the agent was a metallic fragment from a shell, grenade, or mine, which has been called "shrapnel." One man sustained separate bullet wounds affecting major nerves in each arm, so that the series comprises 155 case reports.

DESCRIPTION OF THE CASES

The patients were all sailors or marines whose wounds were sustained in the Pacific theater of war. They reached our hospital on an average of three months from the time of wounding. In this interval they had received excellent care aboard ship or in the various land-based Hospital Units of the Navy, and in general their condition on reaching the mainland was excellent. The number of serious complications was remarkably low. Approximately one-third of these patients were transferred to other hospitals before our studies were completed, and a few additional have been received too recently to permit us to establish a definite prognosis as to spontaneous recovery.

In 40 cases the principal nerve injury implicated the radial nerve; in 20, the median; and in 43, the ulnar. There were 27 instances in which all three major nerves were simultaneously involved; 17 cases represented a combination of median and ulnar; 6, the radial and median; and 2, the radial and ulnar.

In 5 cases the level of wounding was in the neck; 29 were wounded in the axilla; 69 in the upper arm; 12 in the region of the elbow; 36 in the forearm; and 4 were wounded at the wrist.

IMMEDIATE EFFECTS OF WOUNDING

In the immediate history of wounding in these cases, there are four features that occurred with sufficient frequency to acquire significance. These are: (1) a lack of sensation of penetration, and sometimes an absence of any

* The opinions expressed in this article are the private views of the authors and are not to be construed as official or reflecting the views of the Navy Department.

sensation of "impact"; (2) the impression that the extremity has been "blown off"; (3) the occurrence of involuntary contractions in the hand and arm; and (4) a primary phase in which there is both motor and sensory paralysis of the wounded extremity.

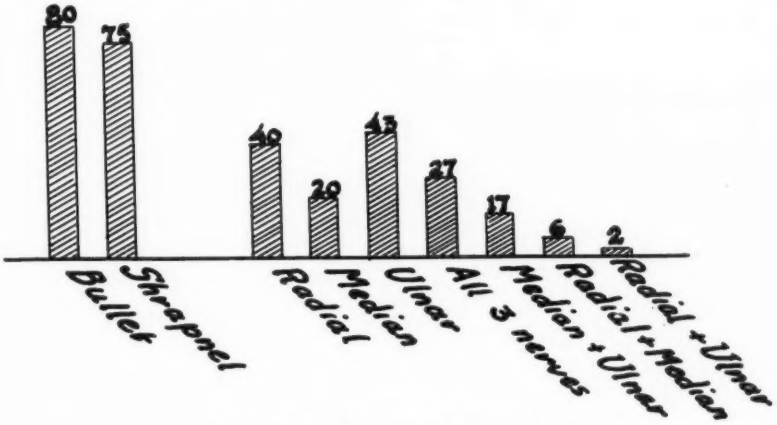

FIG. 1. Wounding agents, and nerves injured.

The majority of men feel the impact of the projectile as a heavy blow with some blunt object. They rarely experience any sense of penetration, and if they have been showered with dirt and pebbles, as in the explosion of a shell,

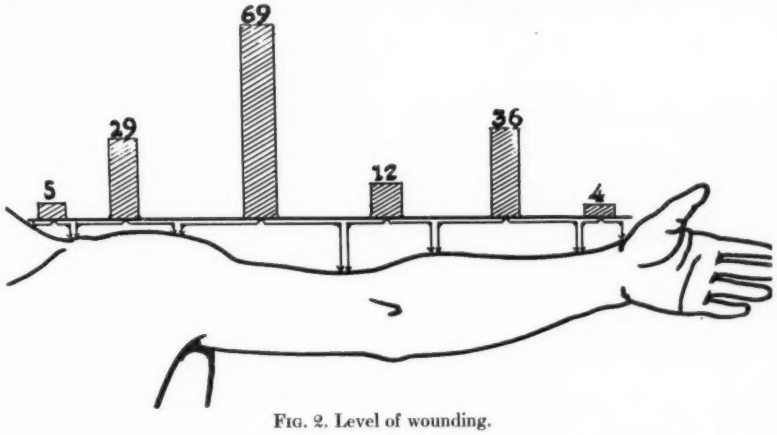

FIG. 2. Level of wounding.

they may be unable to distinguish the impact of the debris from that of the shell fragments. In this series, 26 per cent of the men stated that they did not feel "impact" and were not aware that they were wounded until they saw blood flowing from the arm, or found that the hand would not respond to command.

In 24 per cent of the cases, the wounded man had the impression that his extremity had been "blown off." In some, this impression was so vivid that the man doubted the evidence of his own senses when he saw the limb, or felt it with his normal hand. The patient might be afraid to stand up for fear that the arm, which he saw but could not feel, would fall from his sleeve. This impression of loss of the part was reinforced in a number of instances by some posture of the wounded arm which removed it from sight or placed it beyond his reach. Occasionally, such a distorted posture seemed to be due to a reflex contraction of the muscles. The arm might be drawn back in the hammer-lock position, or stiffly protruded in some fixed posture.

In 32 per cent of the series there was a history of this type of immediate contracture, or else of convulsive movements of the wounded extremity, persisting for several seconds after being hit. One marine found that he could not get up from his prone posture until he had loosened, with his normal hand, the tight grasp of the fingers of his wounded arm on the grass and weeds in which he lay; another man found that the fingers of his wounded extremity were so tightly clasped on the hand grip of his machine gun that he continued to fire the gun involuntarily until the jarring of the recoil bounced his hand off the gun; and a corpsman was certain that his hand had been shot off until he caught sight of it, behind his forearm, sharply flexed at the wrist, jerking in a prolonged series of convulsive movements. Usually, such convulsive movements or muscular contractures were of a few seconds' duration only, and were followed by a flaccid type of paralysis of more lasting nature.

Almost immediately after impact, the hand, and sometimes the arm as a whole, was rendered numb and useless. The extent of this total paralysis usually included the whole extremity to the level of the wound, although it sometimes ascended above the wound, or might be limited to the hand, with partial involvement of the arm to the wound level. Of the men in this series 74 per cent experienced this primary phase of total paralysis as far as the hand was concerned. The duration of the total paralysis varied widely in different cases. A few of the men stated that they were able to move one or more fingers weakly within an hour of the wounding, although the majority of the histories would indicate that the return of any function to the hand required much longer periods of time. In the cases of axillary and neck wounds, and those of the "ischemic" type of paralysis, the hand tended to remain functionless for weeks or months.

SUBSEQUENT EFFECTS OF WOUNDING

As we have related, the immediate effects of wounding varied widely in duration in individual cases, but after the period of total paralysis had passed, a gradual restoration of function appeared in the hand. Usually, some weak movement of one or more fingers appeared before the anesthesia began to fade, while in other patients, particularly in those most severely injured, sensory perception might be partially restored before the slightest

flicker of movement of the fingers was observable. In the men with less serious nerve involvement, a fair degree of motor power returned to parts of the hand within a few hours of wounding, and there were left only the residual evidences of total paralysis of a single nerve. However, the prompt and complete restoration of function to any part of the hand was the exception rather than the rule. The histories elicited from these patients would suggest that the impact of a high velocity projectile, while it might affect one nerve more than others, tended to paralyze nerves at a distance from the actual pathway of the projectile. Since we did not have these men under direct observation during the first months of disability, we have been unable to estimate accurately the duration of the total paralysis occurring in undivided nerves. However, 21 patients still had a complete paralysis of one or more nerves when we first examined them at an average of $2\frac{1}{2}$ months from the time of wounding, and have since (an average of 7 months from wounding) established, or are attaining, a satisfactory return of function. The case histories, as a whole, indicate that the energies released by the passage through the tissues of a high velocity projectile are capable of paralyzing, or at least seriously depressing, for weeks or months, the function of nerves beyond the path of the projectile.

RESULTS OF WOUNDING

It is much too early to estimate the end-results for this series of cases. Three men have been invalided from service with irreparable nerve lesions; 12 have returned to full duty; and 12 have been discharged to limited duty. A return to duty does not always imply a normal restoration of function, and it will be necessary to secure follow-up examinations of these men before their end-results can be finally classified. However, a return to duty does imply that the recovery is definite and progressive, so that the prognosis for a reasonably complete restoration of function appears to be good.

Although the end-results cannot be given at this time, it is possible to secure some information as to progress by the following classification. With the three patients mentioned above as having irreparable nerve lesions, we can group 20 that have been lost from observation, or have come under our care too recently for a prognosis to be established. Exclusive of these 23 patients, there remain 132 who have had sufficient study to permit us to comment on their tendency to recover function spontaneously. Of this group 53 have been subjected to operation, so that we have first-hand information as to the status of the nerves. In only 20 cases was the nerve found to have been completely severed. In 7 additional cases, the operation demonstrated partial lesions, and in 4 of these the surgeon elected to resect the damaged portion and do an end-to-end anastomosis. In 26 cases there was no demonstrable interruption of continuity of the nerves in question. Of the 53 operations, 33 were done at our hospital, and 20 were done elsewhere. It is of considerable interest to note that of the 20 patients operated upon elsewhere, complete severance of the nerve was demonstrated in only 6 (30 per cent).

The remaining 79 patients show signs that seem to indicate that the nerve has not been completely severed. Since there are no reliable signs to distinguish complete severance from "delayed recovery," we may find later that our present interpretations are erroneous, and exploration will show that the nerve has been completely divided. But, for the time being at least, their chances for continued improvement seem to be as good, or better, than we could confer by surgical interference.

Thus, of the 132 patients on whom our studies are reasonably complete, there are 3 discharged with irreparable damage to nerves, 20 proven by

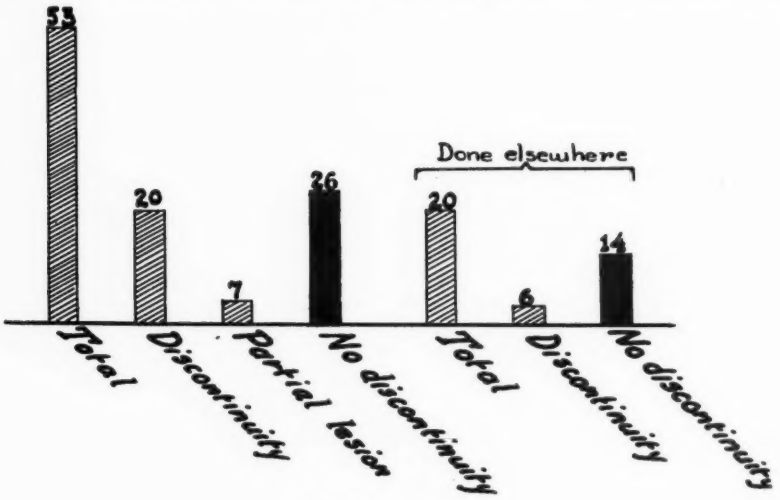

FIG. 3. Operations.

operation to have had the nerve completely severed, and 4 with partial lesions requiring resection of the nerve. The figures from this series would seem to indicate that in wounds due to high velocity projectiles, four out of five of the most seriously damaged nerves escape complete disruption of continuity. If the less seriously damaged nerves, in which the delay in recovery was not so prolonged, were taken into consideration, the ratio would be still higher.

DISCUSSION

High velocity projectiles[2] are known to produce extensive damage to living tissue. The destructive effect that they produce is said to vary as the first power of the mass, and as the cube of the velocity. In other words, given a bullet of a certain mass, passing through a man's arm: to increase its mass three times would be expected to increase its destructive effects three times; to increase its velocity three times, would raise its destructive power twenty-seven times. Apparently the tremendous energies[1] released within the tissues

by the passage of the projectile show a characteristic oscillation of positive and negative pressures, which are transmitted widely through the fluid medium of the tissues, producing injury to structures at considerable distances from the actual path of the projectile. There are doubtless many additional factors that may increase tissue damage, such as the heat of the metallic fragment, "tumble" of the bullet, the lacerating effect of sharp pieces of shrapnel, the angle of incidence, and the density of the tissues traversed. Yet it seems probable that the high velocity of the projectile is the prime factor in causing "delayed recovery" in nerves not actually severed.

Denny-Brown and his colleagues[3,4,5] have reported interesting observations that may have some bearing on our clinical findings. They have shown in experimental animals that various types of local injury to a nerve, such as compression, tapping, freezing or stretching, may be followed by a complete loss of nerve function for weeks or months. If the local lesion is of sufficient severity, the axons of the affected nerve degenerate peripheral to the injury. The axons show no ability to regenerate across the injured segment until all the local damage has been repaired. When the repair process is complete, the axons begin to grow down the distal nerve trunk, progressing at a rapid rate. Because there has been no distortion of the intra-neural pattern by the injury, each fiber eventually establishes connection with its original end-organ. Under these circumstances, as might be anticipated, the recovery of function in these experimental animals approximates the normal. In fact, after some of these experimental "lesions in continuity" the recovery is so complete that it may be difficult even by microscopic examination of the nerve, to tell where the local injury had occurred.

The reaction of nerves to percussion, as demonstrated by Denny-Brown, is strikingly similar to that shown in many of our clinical cases. In each instance, there is a phase of complete paralysis during which it can be demonstrated that the axons peripheral to the level of injury have degenerated. Then, after a variable period of time, depending upon the severity of the lesion, function begins to come back. The eventual recovery of function tends to approximate the normal, presumably because, in each instance, there has been no distortion of the intra-neural pattern.

We have stated that in this series four out of five nerves, seriously damaged by high velocity projectiles, escape anatomic interruption of continuity. In spite of this escape from complete disruption, these nerves sustain profound intrinsic and physiologic changes. In the preliminary portion of the paper dealing with the objective phenomena of wounding, it is implied that transient paralyses may be of a functional nature. It is possible that peripheral nerves subjected to sudden trauma may be capable of creating a state of physiologic block exhibiting phenomena similar to that known as "spinal shock." But we would not expect this form of blockade to persist for long periods. We are of the opinion that *all* nerves that remain functionless for periods of time measured in months will show pathologic changes. In some of

these the pathology may be in the nature of multiple microscopic injuries scattered throughout the nerve trunk for considerable distance. In others, perhaps the large majority, there will be *gross* pathologic changes present. It is possible that some of these nerves with gross lesions in continuity will never recover function spontaneously. In such instances, early resection, followed by an immediate end-to-end anastomosis, is highly desirable.

The difficulty lies in selecting the cases that cannot recover spontaneously, from the larger number that had best be left alone. The surgeon who follows a policy of early exploration realizes this difficulty. He is aware of his responsibility toward his patient in securing the best possible result in the shortest possible time. Yet, in a specific case, he finds himself on the horns of a dilemma. He has no reliable criteria for determining the chances that this particular lesion will or will not preclude an eventual recovery of function. And if he elects to resect the nerve, he has no way of determining the chances of a successful regeneration of the nerve following an end-to-end anastomosis.

The available data concerning the end-results from nerve anastomosis are incomplete and confusing. One can find reports that list the percentage of "failures" all the way from less than 10 per cent to more than 80 per cent. It is our impression that the number of failures will probably lie between 25 and 40 per cent of the total number of nerves sutured, and that the end-results in the remainder leave much to be desired. Some of the factors that militate against full functional recovery are known, such as, inadequate resection of the neuromatous ends, too much tension on the suture line, long delay in carrying out the secondary suture, rotation of the nerve trunk so as to disturb the intra-neural pattern, and damage to the intrinsic blood supply to the nerve. Yet in spite of every effort to overcome these obstacles to success, the surgeon must accept a certain hazard, as far as end-result is concerned, in every case in which he resects a lesion in continuity.

The choice which the surgeon must make at the operating table is between two courses of action, with the outcome predictable in neither one. His first important problem is to decide what the chances may be for a spontaneous recovery. We do not believe that this decision can, with safety, be based solely on the presence or absence of a fusiform neuroma. Denny-Brown's percussion experiments[5] demonstrated that a nerve so injured tends to form a "pseudo-neuroma" at the site, which may persist for as long as twelve weeks. This pseudo-neuroma might be indistinguishable from a true neuroma except by microscopic examination. Yet it does not appear to represent any permanent obstacle to regeneration. In fact, the degree of recovery in his experimental animals tended to approximate the normal, even in cases in which the pseudo-neuroma persisted for weeks and the peripheral portions of the affected nerve remained completely unresponsive to faradic stimulation for long periods of time.

Some surgeons believe that valuable information as to the recoverability

of a nerve can be obtained by perfusing normal saline through the damaged segment. If the resistance to the passage of the fluid through the segment is great, the prospects for spontaneous recovery are assumed to be poor. It has been claimed that if the resistance to the fluid is represented by two or more atmospheres of pressure, the nerve should be resected. This rule of thumb may have some practical value, but to us it has seemed arbitrary and of limited usefulness.

Other surgeons place a considerable reliance upon the response of the nerve to faradic stimulation. If this type of stimulation fails to elicit any motor response in a mixed nerve, it is good evidence that the motor fibers have degenerated peripheral to the lesion. Yet this evidence, taken by itself, is no reliable basis for assuming that the nerve cannot regain function spontaneously. The time factor must be taken into consideration, as well as the level of the nerve injury, i.e., the distance between the site of the lesion and the nearest muscles that that particular nerve supplies. Even when months have elapsed since the wounding, the absence of response to faradic stimulation may not rule out spontaneous recovery. In this series of cases there were three instances of spontaneous recovery in which the nerves failed to respond to a maximal stimulation with a Hinsey-Geohegan stimulator more than five months after wounding. One of these patients had an ulnar paralysis, secondary to a shrapnel wound in the upper third of his forearm. In the fifth month after wounding an exploration failed to demonstrate the exact level of the maximum injury to the nerve. If there had been a single area of gross pathology we doubtless would have resected it, since at operation there was no response of the flexor carpi ulnaris or any of the hand muscles to faradic stimulation. At the end of eleven months the clinical evidence of ulnar paralysis was still complete, and a re-exploration of the nerve was undertaken. Stimulation at this time elicited a contraction of the flexor carpi ulnaris. At the present time, some 15 months from the injury, this patient seems well on the road to a satisfactory recovery of function. This case, and others of a similar nature, lead us to suspect that the microscopic lesions within the nerve trunk may prove to be just as effective obstacles to regeneration as the more obvious gross lesions. However, the point that needs emphasis is the fact that neither the microscopic lesion nor the gross pathology necessarily precludes subsequent regeneration.

CLINICAL APPLICATION

The fact that nerve injuries due to high velocity projectiles show a high percentage of spontaneous recoveries is of some clinical importance. Few surgeons would disagree with the view we expressed less than two years ago, to this effect, "An attempt should be made to do an end-to-end anastomosis on every divided nerve, within the first three weeks of wounding, excepting only those cases of severe, fulminating infection." We had in mind at that time the many advantages of early suture. A successful anastomosis, done

early, not only represents an important reduction in the disability period but, in addition, may result in a more complete restoration of function than could be secured by a later operation. Young[6] has shown that the proliferation of the Schwann cells, so important in the successful re-establishment of nerve continuity, shows an increased growth curve after a nerve trunk has been divided experimentally. The increased activity begins in the first three or four days and reaches its maximum about three weeks later, after which it falls quite rapidly to the original base-line. There are doubtless other factors in the nerve, and in the muscles it supplies, that favor early anastomosis as against the same operation done months later. In all cases in which there is a complete interruption of continuity, there can be no argument against early operation.

In the hands of experts a careful exposure of the lesion should do little harm; complete interruptions of continuity could be repaired immediately; and important observations could be made as to the exact nature of the local lesion. On the basis of such observations it may be possible, eventually, to establish a reliable correlation between certain types of gross pathologic change in the nerve trunk and the prognosis for spontaneous recovery. However, until such a correlation is established, a rigid enforcement of a policy making it incumbent upon all surgeons to explore all nerve injuries within the first few weeks of wounding might do more harm than good.

Our own observations have led away from a rigid policy for early exploration. Our records contain instances in which resections have been done in the absence of convincing evidence that this procedure was indicated. We are increasingly aware that we lack the ability to distinguish, at the operating table and in the early weeks after wounding, the lesions in continuity that are capable of spontaneous recovery, from those that are not. There are,however, a number of conditions that, if present, would influence us to explore the lesion at as early a time after wounding as possible. If the nerve is visualized readily at the time of the original debridement and is seen to be divided, an attempt at suture should be done immediately. If the nerve ends cannot be approximated, they should be fixed to the surrounding tissues by a metallic suture, as close to one another as possible. If the patient suffers from intractable and persistent pain, it may be necessary to explore the wound at an early date. If the projectile passes through such regions as the wrist, the elbow or the musculo-spiral groove, where the nerves are relatively fixed, and hence less likely to escape injury, it would seem advisable to explore early, provided, of course, that the paralysis was complete. Exploration of these sites would be especially indicated when the injury was complicated by fracture of the adjacent bone. But if the wound occurs in areas where the nerve is not fixed, if the theoretical path of the projectile between the wounds of entrance and exit do not correspond exactly to the nerve location, and particularly when the wounding agent is a high velocity projectile, it is certainly justifiable, and perhaps indicated, to delay exploration until a period of study and a careful evaluation of the case has been completed.

CONCLUSION

Unless there is more evidence than a simple loss of nerve function, to suggest that a nerve has been severed, a period of observation of two or three months seems indicated in the treatment of nerve lesions caused by high velocity projectile wounding.

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VENTRICULOGRAPHIC DIAGNOSIS OF CYSTICERCOSIS OF THE POSTERIOR FOSSA

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CYSTICERCOSIS is a result of the encystment of the larvae of Taenia solium or Taenia saginata in the tissues of different kinds of animals. Usually man harbors the adult taenia, but under certain conditions he may become the intermediary host, harboring the larvae.

Taenia saginata is as common as Taenia solium. The predominance of one or the other type of parasite in human infestations is related chiefly to the kind of food ingested. Thus there is a higher rate of infestation by Taenia solium in Germany where pork is eaten mainly, and by Taenia saginata in those countries where beef is the common meat. In Chile there are more Taenia saginata cases in the cities, whereas Taenia solium cases are more frequent among the rural population. Nevertheless, Cysticercus bovis is extremely rare and there is doubt that it has ever been observed in man. The literature records only one case. Actually, then, human cysticercosis may be said to be due exclusively to Taenia solium.

The life cycle of the parasite is well known. It is granted that once embryonic eggs reach the stomach through ingestion of contaminated food or drink, auto-infection through dirty hands, or possibly regurgitation in an individual harboring an adult taenia, these are digested and the embryo, being freed, proceeds to bore its way through the intestinal wall and thus enters the portal or the lymphatic system, thence reaching the general circulation.

Although it is not the purpose of our work, let us point out some interesting facts. Cysticercus cellulosae shows a great preference for the central nervous system and its coverings. Its hepatic or pulmonary localization is rare. On the other hand, the hydatid, which enters the circulation in the same way, localizes itself usually in the liver and frequently in pulmonary tissues. It is rarely found in the nervous system.

Two observations throw some light on this question of preferences for certain tissues. (1) We have observed cysticerci of the nervous system associated with localizations in the skin. The subcutaneous cysticerci were small and appeared and disappeared in from 15 to 25 days. Death of the larva was confirmed by histological examination. (2) In the brain itself we have

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been able to observe, especially in cases where the fourth ventricle and posterior fossa were involved, numerous dead cysticerci whose destruction was histologically confirmed.

This has led us to think that the human organism may produce special substances that destroy the cysticerci. It is conceivable that the amount of these substances might vary in different tissues, thus explaining the more frequent invasion of the eye and brain. This possibility is being investigated at the Institute.

LOCALIZATION OF CYSTICERCI

A brief historical résumé may be given. Trelles and Lazarte[11] cite Dressel (1877) who found that in 87 cases of cysticercosis the brain was affected in 72 (82 per cent); Stiles (1906) who in 155 cases found cysticerci in the brain in 117 (75 per cent); and Vosgien (1911) who reported that in 807 cases the brain was affected in 330 (40 per cent). The highest percentage of the figures above, therefore, correspond to localization in the central nervous system.

Krause[7] reported that Küchenmeister in 88 cases of brain cysticercosis found the meninges involved in 49, the cortex in 59, and the ventricles in 18. When the ventricular system was invaded the fourth ventricle was most often affected. Only in 19 cases were cysticerci seen deep in the white matter.

Localization in the ventricles is very frequent. Sato,[10] for instance, in 128 cases of brain cysticercosis found 48 examples (38 per cent), 22 of which were cysts of the fourth ventricle.

At the Instituto Central de Neurocirugía we have had, during a period of three and a half years, 25 cases of brain cysticercosis in a total of 202 intracranial tumours. This gives an idea of the practical importance of this condition. As will be shown later, the percentage of localization in the posterior fossa is very high.

DIAGNOSIS OF CYSTICERCOSIS OF THE BRAIN

The purpose of this paper is to throw some light on the diagnosis of this important medical problem. The diagnosis of cysticercosis is difficult. The clinical picture is variable and obscure. Trelles and Lazarte,[11] Henneberg[6] and Lopez Albo[8] have given excellent descriptions. In spite of their complexity, the signs and symptoms found constitute one of the bases of the diagnosis. Certain biological procedures yield valuable data in cysticercosis of the brain but in most instances they are of little use in arriving at the correct diagnosis. Recent publications mention this problem and Hare[5] says: "Premortem diagnosis is often difficult; the condition may be revealed only at autopsy." This is quite explainable because of the scarcity of this affection in the United States.

The X-ray has been useful. All the publications that we have been able to consult, when referring to X-ray diagnosis, take into account the images formed by the calcified cysticerci. Thus Henneberg describes small clear images, numerous, rounded and homogeneous. The tumours, he states, if

calcified appear more granulated with less clearly defined contours. Brailsford,[1] in an article on the diagnosis of Cysticercus cellulosae in the muscles and in the central nervous system, refers only to this type of picture. Calcification is, therefore, the only possible means of revealing the cysticercus in simple X-ray plates. It is interesting to recall that, according to Dixon and Smithers,[2] in 71 cases of intracerebral cysticercosis the cysticerci calcification in the brain was found only three times by X-ray.

As to ventriculography, the literature is poorer. We have at our disposal only isolated reports of ventriculographic interpretations. One is the case of Heymann, whose ventriculograms were reproduced in Henneberg's work.[6] Another is that of Grana and Schenone[4] in which the authors describe a suspicious image of the third ventricle and of the right occipital horn. Fracassi, Babbini and associates[3] present a careful encephalographic study but refer only to its localizing values; the same is true of the report by Ray in 1941.[9] All ventriculograms published relate exclusively to supratentorial localizations. Usually supratentorial cysticercosis is intraparenchymal (encysted). This is not true of cysticercosis of the posterior fossa cisternae, where racemose clusters ("bunches of grapes") are found.

In our experience localization in the ventricular cavities and cisternae of the infratentorial region is much more frequent. In 25 cases of brain cysticercosis, we have been able to study 22 series of ventriculograms (representing 20 ventriculographies and 2 encephalographies). There were 20 cases of infratentorial cysticercosis: in 13 the predominant localization was in the posterior fossa and in 7 there was a single cysticercosis of the fourth ventricle. All were verified either surgically or by autopsy. The results of the ventriculographic studies in each group are given in the following case reports.

VENTRICULOGRAPHY IN CYSTICERCOSIS OF THE POSTERIOR FOSSA

(Thirteen Cases)

Case 1. E.T., female, aged 37. Admission: Aug. 4, 1940. Symptomatology of vertigo and tinnitus. Since 1938 progressive headaches associated with vomiting. Vision right eye 4/24; left eye can only distinguish movement.

Ventriculogram: Dilated ventricular system. Aqueduct of Sylvius is visible only for an extent of about ½ cm. from its opening in the third ventricle. Good filling of the fourth ventricle, at least in its upper part. There is also air in the posterior fossa, as can be clearly seen in Figs. 1 and 2. The rest of the plates show no displacement of the aqueduct.

Operation: Sept. 17, 1940. Decompression of the posterior fossa. Disclosure of racemose cysticercosis.

Discharge: Nov. 12, 1940. The patient died in January 1941 at home.

Case 2. J.M.A., male, aged 41. Admission: June 2, 1941. History of tinnitus, vertigo and convulsive seizures. Headache and vomiting for a year. Slow cerebration. Bilateral choked disc.

Ventriculogram: Marked dilatation of the ventricular system. Aqueduct of Sylvius and fourth ventricle are not visible. Good filling of the posterior fossa.

Operation: June 13, 1941. Decompression of the posterior fossa. Disclosure of racemose cysticerosis.

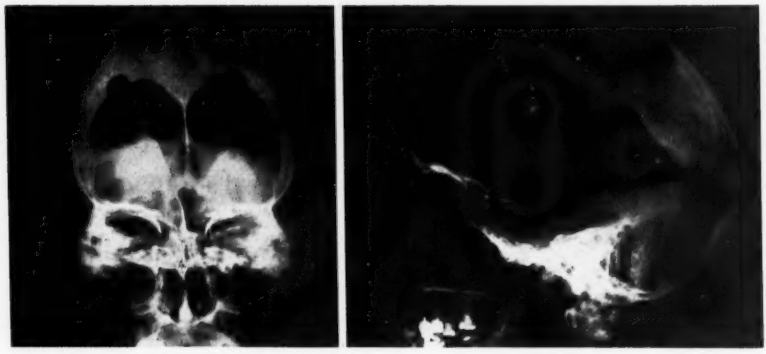
Death Aug. 4, 1941. Autopsy: Hydrocephalus; racemose cysticercosis.

Case 3. R.H.S., female, aged 45. Admission: Aug. 15, 1941. For 11 years, vertigo, tinnitus and diminution of visual acuity. For 5 years, vomiting. For 3 years, headache. Left eye: optic atrophy; right eye: choked disc.

Ventriculogram: Picture similar to Cases 1 and 2 with air passage to the posterior fossa and poor visualization of the aqueduct.

Operation: Aug. 26, 1941. Suboccipital decompression. Disclosure of racemose cysticercosis.

Discharge: Oct. 21, 1941.



FIGS. 1 and 2. Case 1. Ventriculograms showing good filling of the fourth ventricle. No displacement of the aqueduct.

Case 4. R.S.Z., male, aged 38. Admission: Oct. 9, 1941. For 2 years, headache, tinnitus, vomiting, lumbago, staggering gait, and loss of vision. Bilateral choked disc.

Ventriculogram: Ventricular system greatly dilated. Enlargement of the aqueduct and fourth ventricle. Good filling of the posterior fossa.

Operation: Oct. 17, 1941. Suboccipital decompression.

Death Nov. 13, 1941. Autopsy: Hydrocephalus and racemose cysticercosis of the posterior fossa.

Case 5. M.C.C., male, aged 40. Admission: Nov. 25, 1941. Headache, vomiting, tinnitus, staggering gait, failing memory and slow cerebration for 2 years. Choked disc.

Ventriculogram: Aqueduct of Sylvius occupied by air in its initial portion. After a tract of 2 cm. its shadow becomes invisible. Plenty of air in the posterior fossa.

Operation: Jan. 2, 1942. Suboccipital decompression. Obliteration of the aqueduct. Racemose cysticercosis.

Death Feb. 2, 1942. Autopsy: Racemose cysticercosis.

Case 6. N.C., female, aged 42. Admission: Jan. 26, 1942. For 10 years diplopia, vertigo, staggering gait and tinnitus. Choked disc.

Ventriculogram: Bilateral and symmetrical enlargement of the lateral ventricles. Aqueduct of Sylvius obstructed. Fourth ventricle is visible. Good filling of the posterior fossa.

Operation: Feb. 10, 1942. Decompression of the posterior fossa. Racemose cysticercosis.

Discharge: Feb. 15, 1942.

Case 7. A.B.S., male, aged 39. Admission: Feb. 9, 1942. Headache, vomiting, diplopia, tinnitus and staggering gait since 1940.

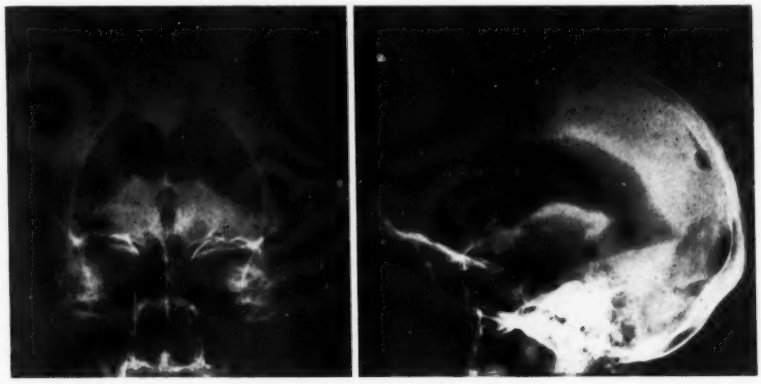
Ventriculogram: Great and symmetrical dilatation of the lateral ventricles with enlargement of the third ventricle and the aqueduct. Fourth ventricle cannot be seen and there is no air in the posterior fossa.

Operation: April 13, 1942. Suboccipital decompression.

Death April 17, 1942. Autopsy: Hydrocephalus; racemose cysticercosis.

Case 8. P.A.D., male, aged 34. Admission: May 6, 1942. Onset of disorders in 1940 with headache, vomiting, dizziness, tinnitus, slow cerebration and failure of vision. Atrophy due to choked disc.

Ventriculogram: Outlet of the aqueduct of Sylvius perfectly visible with embossment-



FIGS. 3 and 4. Case 8. Anteroposterior and lateral ventriculograms showing outlet of the aqueduct of Sylvius with embossment-like deformities, which gradually enlarges to form the fourth ventricle. Air in the cisterna cerebellum medullaris.

like deformities, gradually enlarging to form the fourth ventricle (Figs. 3 and 4). There is air in the posterior fossa which is more plainly visible in position 7 of Lysholm. In position 3 of Lysholm there is a shadow in the pia-arachnoidal space that suggests an arachnoidal cysticercosis process. This image can be seen in the simple X-ray plate.

Operation: May 19, 1942. Suboccipital decompression. Racemose cysticercosis.

Discharge: June 29, 1942.

Case 9. C.T.T., male, aged 33. Admission: Aug. 24, 1942. Headache, slow cerebration, vomiting, failing vision, left hemiparesis, vertigo, staggering gait and tinnitus for 5 years. Optic atrophy.

Ventriculogram: Ventricular system grossly dilated. Aqueduct of Sylvius is clearly visible, but not the fourth ventricle. There is air in the posterior fossa.

Operation: Oct. 6, 1942. Suboccipital decompression. Racemose cysticercosis.

Death Oct. 13, 1942. Autopsy: Racemose cysticercosis.

Case 10. E.Z.I., female, aged 46. Admission: Mar. 15, 1943. Since 1940 headache, vomiting, euphoria, dimness of vision, vertigo, deafness and tinnitus of the right ear. Choked disc.

Ventriculogram: General enlargement of the ventricular system maintaining its normal position. Aqueduct is visible at its opening in the third ventricle. After a tract of $1\frac{1}{2}$ cm. it vanishes, due probably to a partial obstruction, since there is plenty of air in the posterior fossa.

Operation: Mar. 10, 1943. Decompression of the posterior fossa. Racemose cysticercosis.
Discharge: May 20, 1943.

Case 11. R.L.C., male, aged 42. Admission: June 21, 1943. Progressive disorders for 6 years with headache, vomiting, slow cerebration, dizziness, trembling, and failing of the visual acuity. No choked disc.

Ventriculogram: Great dilatation of the ventricular cavities. Aqueduct is visible to 1 cm. from its outlet. There are air bubbles in a zone corresponding to the fourth ventricle. Poor filling of the posterior fossa.

Death July 22, 1943. Autopsy: Racemose cysticercosis.

Case 12. J.T.A., female, aged 38. Admission: Oct. 11, 1943. Successively since onset 4 years before, headache, vomiting, numbness of the left side of the face, convulsive seizures associated with loss of consciousness, dizzy spells, tinnitus, failing vision and left hemiparesis. Choked disc.

Ventriculogram: Bilateral and symmetrical enlargement of the lateral ventricles and dilatation of the third ventricle and aqueduct. The fourth ventricle appears dilated. There is plenty of air in the posterior fossa.

Operation: Nov. 23, 1943. Suboccipital decompression.

Patient discharged Jan. 14, 1944 in very good condition.

Case 13. A.B.C., male, aged 34. Admission: Dec. 20, 1943. For 6 months headache, vomiting and slow cerebration; gastrointestinal disorders for last month. Choked disc. Left hemiparesis.

Ventriculogram: Bilateral and symmetrical dilatation of the ventricular cavities. No visualization of the aqueduct of Sylvius. Good filling of the posterior fossa.

Operation: Jan. 14, 1944. Suboccipital decompression. Racemose cysticercosis.

Death Jan. 14, 1944. Autopsy: Racemose cysticercosis.

Comment. From the cases reported it may be derived that cysticercosis of the posterior fossa gives a ventriculographic picture similar to that caused by tumours occurring in this region, i.e., (a) bilateral hydrocephalus of the whole supratentorial system; (b) slight and symmetrical dilatation, with only some variations in form; (c) dilatation of the foramen of Monro; (d) dilatation of the third ventricle with maintenance of suprapineal recess, anterior commissure, posterior commissure and massa intermedia.

However, a careful study of the ventriculograms in cases of cysticercosis reveals a special appearance that is of assistance in reaching a pre-operative diagnosis. This is important since the disease is usually incurable. Only if there is evidence of a single cysticercus or a localized collection is there a chance that the patient can be cured. This is true when dealing with single cysticercosis of the fourth ventricle.

Cysticercosis of the posterior fossa produces three principal lesions that are the basis of X-ray diagnosis: (1) partial obliteration of the aqueduct of Sylvius, fourth ventricle and cisternae by the cysts; (2) arachnoiditis; (3) toxic and diffuse encephalitis associated with cerebellar atrophy.

Any intracerebellar tumour means an expanding and progressive process that sooner or later causes a complete obliteration of the aqueduct. According to its localization, displacement of this channel is upwards, downwards, to the right or left, forward or backward. It has a characteristic appearance: the obliterating point is outlined definitely and precisely. Passage of air to

the posterior cisterna is rare. In cysticercosis the picture is very different: the characteristics are (a) dilatation of the aqueduct of Sylvius (up to 1 cm.) with absence of deviation; (b) only partial obliteration of the aqueduct—there is always some filling of the aqueduct and fourth ventricle; (c) good passage of air to the cisterna magna; (d) presence of air around the cerebellum as a consequence of the atrophy of that region.

These facts are based upon a study of the 13 cases reported above. It is possible to make a diagnosis of cysticercosis before operation if one considers the clinical picture together with the X-ray findings as described.

VENTRICULOGRAPHY IN SOLITARY CYSTICERCOSIS OF THE FOURTH VENTRICLE

(Seven cases)

Case 14. M.R., female, aged 46. Admission: May 16, 1940. Successively since onset 2 years before, headache, diplopia, failing vision, vomiting and vertigo. Normal visual field for one year. Choked disc.

Ventriculogram: Bilateral and symmetrical hydrocephalus. Irregular filling of the fourth ventricle. Aqueduct is visible only at its opening in the third ventricle.

Operation: June 21, 1940. Suboccipital decompression. Cysticercosis of the fourth ventricle.

Death June 24, 1940. Autopsy. No other cysticercus found in rest of the body.

Case 15. E.Z.T., female, aged 22. Admission: July 2, 1940. Headache for 3 years and diplopia for one year. Bilateral choked disc.

Ventriculogram: Slight dilatation of both ventricular cavities. Aqueduct of Sylvius is not visible. Air present in the fourth ventricle and the posterior fossa.

Sudden death Aug. 31, 1940. Autopsy: Single cysticercosis of the fourth ventricle. No other parasite found in rest of the body.

Case 16. O.C., male, aged 33. Admission: Oct. 17, 1941. Symptoms of headache, vomiting and stiff neck. Since 1939 diplopia and staggering gait. Diabetic disorders persisted after treatment. Choked disc.

Ventriculogram: Bilateral and symmetrical hydrocephalus of the ventricular system. Obstruction of the aqueduct in its outlet from the third ventricle. Presence of air in its inferior part, which is dilated. Dilatation of the fourth ventricle and the posterior fossa.

Operation: Nov. 14, 1941. Suboccipital decompression. Excision of a single cysticercus from the fourth ventricle. No parasites in the rest of the cavities.

Discharge: Dec. 13, 1941.

Case 17. E.S.M., female, aged 25. Admission: Oct. 10, 1941. For 4 months headache, humming ear, vomiting, singultus and vertigo. Bilateral choked disc.

No ventriculogram.

Operation: Oct. 21, 1941. Suboccipital decompression. Cysticercosis of the fourth ventricle.

Death: Oct. 22, 1941. Autopsy: No parasites in rest of the tissues.

Case 18. M.Q.Y., female, aged 41. Admission: Oct. 1, 1943. Complaint of vomiting, stiff neck, and headache for 2 years. Bilateral choked disc.

No ventriculogram—the patient died suddenly the night before scheduled operation.

Death: Oct. 4, 1943. Autopsy: Solitary cysticercus of the fourth ventricle (Fig. 5). No parasites in rest of the tissues.

Case 19. J.L.V., male, aged 24. Admission: Sept. 7, 1943. Vertigo, headache and stiff neck for a month. No choked disc. Normal mentality.

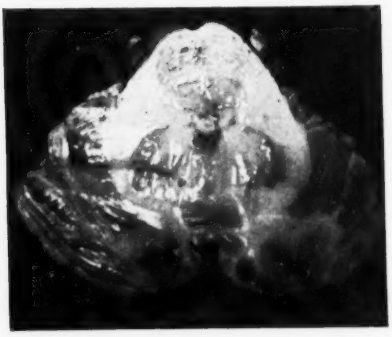
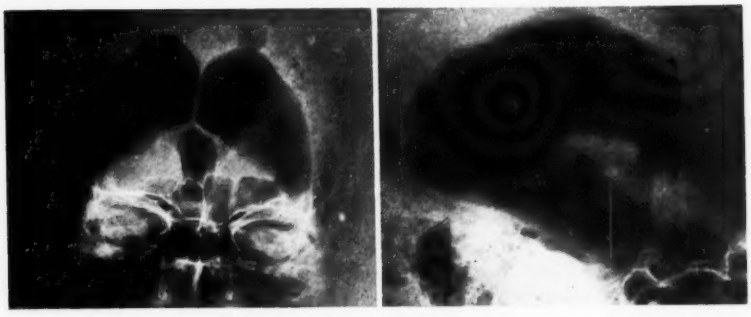


FIG. 5. Case 18. Single cysticercus of the fourth ventricle.



FIGS. 6 and 7. Case 19. Ventriculograms showing enlargement of the aqueduct, which is obstructed in a tract of 1½ cm. from its opening in third ventricle. Dilatation of the fourth ventricle. Air around the cerebellum and the cisterna cerebellum medullaris.

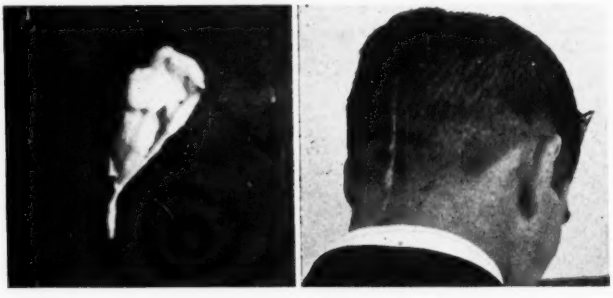


FIG. 8 (*left*). Case 19. Single cysticercus removed from the fourth ventricle and aqueduct of Sylvius.
FIG. 9 (*right*). Case 19. Patient nine months after operation.

Ventriculogram: Ventricular system grossly dilated. Dilatation of the aqueduct, which is obstructed in a tract of 1½ cm. from its opening in the third ventricle (Figs. 6 and 7). Marked dilatation of the fourth ventricle.

Operation: Oct. 15, 1943. Suboccipital decompression. Solitary cysticercus of the fourth ventricle (Fig. 8). Atrophy of the cerebellum.

Discharge: Nov. 17, 1943. Follow-up examination: July 1944. Patient in good condition (Fig. 9).

Case 20. G.G., female, aged 30. Admission: Nov. 28, 1943. Headache, vomiting, staggering gait and failing vision since childhood. Anosmia for 2 years. Bilateral choked disc.

FIG. 10 (*left*). Case 20. Good filling of the aqueduct in a tract of ½ cm., which is dilated. Air in the cisterna cerebellum medullaris.

FIG. 11 (*right*). Case 20. Patient six months after operation.

Ventriculogram: Bilateral and symmetrical hydrocephalus. Good filling of the aqueduct in a tract of ½ cm., which is dilated. Presence of air in the cisterna magna (Fig. 10).

Operation: Dec. 3, 1943. Suboccipital decompression. Marked arachnoiditis. Solitary cysticercus of the fourth ventricle. No parasites in the rest of the cavities.

Discharge: Jan. 6, 1944. Follow-up examination: July 1944. Patient in good condition (Fig. 11).

Comment. The ventriculograms in cysticercosis of the fourth ventricle reveal a picture similar to that in cysticercosis of the posterior fossa. Complete obliteration of the aqueduct is rare, while practically always there is free passage of air to the cisterna magnus. In two cases we have been able to see the outline of the cysticercus within the aqueduct.

SUMMARY

Twenty cases of brain cysticercosis have been studied by ventriculograms obtained by injection of air. In 13 the predominant localization was in the posterior fossa and in 7 there was a single cysticercosis of the fourth ventricle. All were verified either surgically or by autopsy.

The X-ray findings that point to cysticercosis of the posterior fossa are: 1) hydrocephalus, 2) absence of displacement of the ventricular system, especially of the aqueduct, and 3) partial obliteration of the aqueduct and fourth ventricle with presence of air in both and in the cisterna magna. These

same features can be observed in cases of single cysticercosis of the fourth ventricle. In the latter the contours of the cysticercus may be outlined.

Ventriculography, associated with careful clinical, biological, and laboratory examinations, is the most valuable method for reaching an accurate localizing diagnosis in cysticercosis of the posterior fossa.

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CYST OF THE SIXTH VENTRICLE (CAVUM OF VERGA) SUCCESSFUL REMOVAL THROUGH TRANSVENTRICULAR APPROACH WITH NOTES ON EMBRYOLOGY AND HISTOPATHOLOGY*

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THERE have been many reports of cysts of the septum pellucidum (5th ventricle), but descriptions of cysts of the ventricle of Verga (6th ventricle) are rare.

The cavity of the 6th ventricle was first described by Andrea Verga, an Italian anatomist, in 1851. Other names given for this cavity are: Verga's

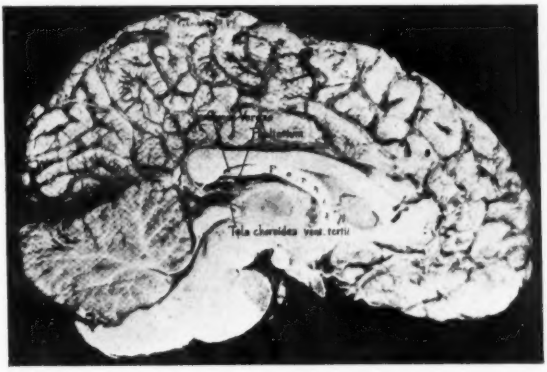

FIG. 1. Small, slit-like cavum Vergae (6th ventricle). Boundaries: anteriorly, the anterior limit of the fornix; superiorly, the body of the corpus callosum; posteriorly, the splenium of the corpus callosum; inferiorly, the psalterium (lyra Davidis) and the hippocampal commissure. (From Dandy[2])

ventricle, 6th ventricle, ventricle of Strambio, ventriculus fornicis, ventricularis triangularis and canal aqueduc. The reader is referred to Dandy's article for an excellent historical summary.[1]

It is claimed that the combined cavity of the septum pellucidum and Verga is found as a small, non-pathogenic space in 2.5 per cent of brains examined at necropsy.[1] Corning stated that in the adult an extension of this lumen as far caudally as the splenium is present in 3 per cent of all brains, and Verga observed that these cavities are found only in the human species.[1,2,7]

* Presented before the Philadelphia Neurological Society, November 1943.

The boundaries of the cavum of Verga are as follows: Anteriorly, the anterior limit of the fornix; superiorly, the body of the corpus callosum; posteriorly, the splenium of the corpus callosum; and inferiorly, the psalterium (lyra Davidis) and the hippocampal commissure. The cavity is also triangular when viewed laterally (Fig. 1) and flares out laterally on both sides with the curve of the fornix pushing in the lateral ventricles at the extreme lateral extensions (Fig. 2). The floor of the cavity rests on the tela choroidea (Fig. 3).

It is stated that either cavity may be present without the other, both may co-exist and be independent, or they may communicate with each other through openings in the fornix (Figs. 2 and 3). However, Van Wagenen and Aird believe that embryologically, the cavities are one and only chance variations in development may separate them, the cavum of Verga being simply the most posteriorly drawn-out portion of the cavity of the septum pellucidum.[6]

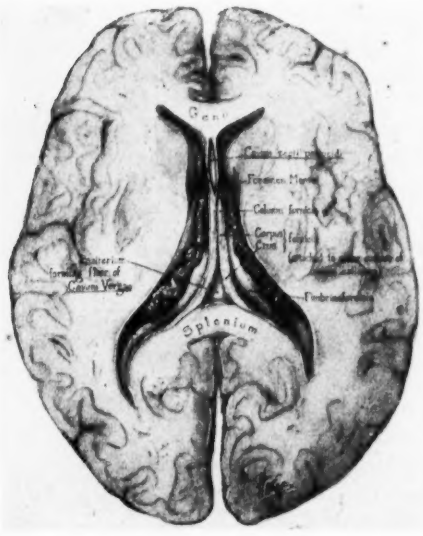

FIG. 2. Cavum septi pellucidi and cavum Vergae, each independent. The cavum Vergae is also triangular when viewed laterally and superiorly. (From Dandy[2])

Wolf and Bamford published an excellent report on the embryology and histopathology of these cysts.[7] They quote two main embryological theories of origin: One theory contends that the rapid widening of the lamina terminalis in the third fetal month produces internal tensions with the formation of a cavity within its substance (Streeter, G. Elliott, Smith, Marchand). The other theory, proposed by Corning, considers the cavity to be a portion of the inter-hemispheric fissure whose lateral boundaries are the medial aspects of the cerebral vesicles, ventral to the caudally extending corpus callosum. He contends that the cavity reaches back to the splenium in the seventh fetal month, the caudal end of the cavity being greatly obliterated by the union of the floor with the corpus callosum. This would explain the much higher frequency of a patent anterior cavum or cavum septi pellucidi without any cavum posticus or Vergae. Dejerine also links the development of these cavities with that of the inter-hemispheric fissure.[7]

There has been a controversy as to whether these cavities are true parts of the ventricular system. Dandy states that neither cavity is part of the ventricular system. He believes that the openings in the cyst that communi-

cate with the ventricles are artificial, because they are inconstant in position, size and number and especially because the borders of these openings are ragged and uneven.[1] He quotes Verga as stating that Petit and Wenzel, Trideman, Michel and Valenin considered the openings between the cavity of the septi pellucidi and the ventricular system to be normal. Vic d'Azyr and Santorini, as well as Verga, thought that they were artificial. No one has ever reported finding remnants of the choroid plexus in these cavities or cysts.[1]

Van Wagenen and Aird divided the cavities into three groups: 1) Noncommunicating—the wall intact and the cavity closed. 2) Communicating—with the adjoining third or lateral ventricles as a result of rupture of walls when fluid pressure from within reaches a certain point. 3) Secondary or acquired dilatations of the communicating type as a part of a later development or superimposed hydrocephalus, from whatever cause.[6]

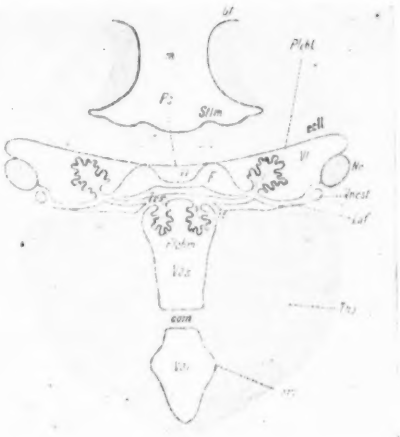

FIG. 3. Diagram from Obersteiner showing the relation of the 6th ventricle (ventricle of Verga) to corpus callosum from above and psalterium below. *cell* corpus callosum; *F* fornix; *Ps* psalterium; *VV* 6th ventricle; *V3* third ventricle; *Vl* lateral ventricle; *Plch* choroid plexus.

The origin of fluid in these cavities or cysts is not known. There are no published analyses of the microscopic and chemical contents of the fluid. Testut and Reichert have suggested a transudate from the lateral ventricles as a source of the fluid.[7]

Van Wagenen and Aird suggest that embryonic rests of pia arachnoid in the inner walls of the septum might be the origin of the fluid, although they have not been able to show this histologically.[6] Wolf and Bamford state that, although this suggestion appears embryologically sound, the histological findings in their cases are against this theory. It is possible, they add, that mesodermal elements probably included in the embryological development of the cavi disappear.[7] Dandy also states that inclusions of choroid plexus in the cyst wall have been suspected but never demonstrated.[2]

Reports on the histopathology of cysts of the sixth ventricle are extremely rare. Wolf and Bamford have studied very thoroughly an excised cavity of the septum pellucidum and cavum Vergae, obtained as an incidental finding at autopsy of a 74 year old woman:

> The major portion of the wall of this combined cavity was composed of a mat of glial fibers in which moderate numbers of fibrillary astrocytes with scant cytoplasm was present. Occasionally, such a cell lay flattened on the surface. In each section, there were from three to

five strips of cells, single-layered, scattered along this glial surface, covering only a very inconsiderable portion of it. The cells varied from low to high cuboidal form. The cytoplasm was finely granular and lightly acidophilic. The nuclei were large, oval or spherical and centrally placed. The external and internal limiting membranes of the cells were quite distinct. The glial network on which the rows of cells were supported consisted of dense masses of glial fibers, most of them parallel to the surface of the cavity. None of the cells had any cilia or contained blepharoplasten.

Against these cells being true ependymal cells, they believe, is the fact that they do not form a complete membrane, like ependyma, that no blepharoplasten have been demonstrated in them, and finally, that the cavi are not considered part of the ventricular system. No collagen fibers or any cells that seemed to be mesodermal in origin were found anywhere along the lining of the cavity. They admit that it is possible that the mesodermal elements that are probably included in the embryological development of the cavi disappear.

Wolf and Bamford have also examined a series of human embryos to determine whether cells similar to those described in the adults lined the cavities in the fetus. No such cells were found in a series extending from a four weeks embryo to a baby at term.

The writer could find no report in the literature of a successful removal of a cyst of the ventricle of Verga. Dandy (1931) reported two operative cases. In one, a woman 50 years of age, he decompressed a combined cyst of the septum pellucidum and Vergae by puncturing the wall of the cyst and permitting communication with the lateral ventricle. No biopsy was taken of the cyst wall and the patient died three weeks later. His second case was of a boy, four and a half years of age, and appears to be one of a cyst of the septum pellucidum rather than the ventricle of Verga. Here, again, the cyst wall was decompressed. No biopsy was reported. When seen eight months after the operation, the child was considerably improved.[1,2]

Van Wagenen and Aird (1934) reported one case of cyst of the septum pellucidum with decompression into the lateral ventricle. No biopsy specimen is reported. They also reviewed two cases of cyst of the ventricle of Verga; in one (Case 14) a suboccipital craniectomy was done and at autopsy a dilated cavum pellucidum and cavum of Verga were found. In the second (Case 15) a ventriculogram done on a six week old infant suggested a cyst of the ventricle of Verga. A cerebellar exploration was also done in this infant and adhesions found in the posterior fossa. No histological or necropsy findings were reported.

Love, Camp and Eaton (1938) reported a case of symmetrical cerebral calcification, particularly of the basal ganglia, associated with a cyst of the cavum septum pellucidum. At operation they resected the cyst wall in this area. From their description, it is not clear whether they removed just one wall of the sac or the entire sac. The patient died on the eighth day postoperatively. Necropsy showed that the cavum septum pellucidum and cavum Vergae were continuous and about equally dilated, measuring 12 mm. in transverse diameter at a point of attachment to the walls of the corpus cal-

losum. There is no histological report of the cyst wall they removed except a statement that remnants of the choroid plexus could not be found in the walls of the cyst.[5]

Leslie reports a case of a man, 44 years of age, in whom air studies showed a defect in the superior portion of the third ventricle. A transcallosal operative approach was done and a thin membrane, resembling omentum, was found in and below the corpus callosum. It appeared to be a cyst wall. The fluid in it appeared to be clear. No attempt was made to remove the mass but a biopsy was taken of the softened corpus callosum and cyst wall. There was no histological report. Air studies taken three years later still showed the same defect as before operation.[4]

CASE REPORT

B.M., female, aged 6, was referred by Dr. Samuel Polcino to the Neurosurgical Clinic at the Northeastern Hospital on November 12, 1942 with a history of recent headaches and convulsions. At three months of age the child had twenty-two convulsions in three days. She remained well until 4½ years of age when she would complain of attacks of headache and vomiting. Between these episodes the patient appeared normal to the parents until six weeks before the present examination, when she had severe headaches and convulsions. The mother noticed that, at times, the attack would start on the right side, that the movements were clonic in type and that only feeble movements occurred on the left side. The child would quickly recover from the seizures with no residual symptoms.

The birth history was normal. She sat up at eight months, talked at nine months, but did not start to walk until 23 months of age. There is no history of other illnesses.

Family history: The patient's sister, aged 2½ years, also had three generalized convulsions when four months of age. However she has had none since and examination (at this writing) shows an apparently healthy child with no hydrocephalus.

Examination. Dr. Alexander Silverstein, attending neurologist, noted: "The head is enlarged (circumference 56 cm.). The cranial nerves are negative. The tendon reflexes are normal. There is a slight ankle clonus bilaterally. There is no Hoffmann sign and no Babinski sign. Sensation, including stereognosis, is not impaired. Cerebellar tests are well performed. Although there is no definite motor impairment, there is a suggestion that the right upper and lower extremities are weaker than the left. The striking feature is the relative absence of mental and neurologic signs in the presence of a marked hydrocephalus."

Dr. Granville Lawrence, attending ophthalmologist, reported: "The pupils are equal and react well to light and accommodation. A convergent strabismus is present. There are full rotations in all meridians. The patient fixes with the left eye; the right eye is turned in about 30°. The eye grounds are negative. The strabismus is probably on the basis of a refractive error."

Blood Wassermann was negative. Spinal fluid studies were: no cells, sugar 61 mg., protein 50 mg., chlorides 775 mg. per 100 cc.; Wassermann and colloidal gold tests were negative.

A psychometric examination (Stanford-Binet test) by Dr. John Lachman revealed a mental age of 6½ years. X-ray showed an enlargement of the skull.

An encephalogram was done on February 18, 1943 under avertin and ethyl-chloride anesthesia. The initial pressure was 18 mm. of mercury in the horizontal position; 240 cc. of fluid was removed and 220 cc. of air injected. The air studies showed a large cavity filled with air projecting into the mesial walls of both lateral ventricles (Figs. 4, 5 and 6). Both lateral ventricles were markedly enlarged, the right more so than the left. On lateral view, a large cavity, filled with air and surrounded by a membrane, could be seen in the region of the corpus callosum. This finding suggested the presence of an extra cavity that contained fluid and probably communicated with the third ventricle. Since the septum pellucidum showed

FIG. 4. Encephalogram (author's case) showing a huge cavity filled with air projecting into the mesial part of both lateral ventricles but more to the right. Note marked enlargement of ventricles due to partial obstruction by cyst of the foramina of Monro and probably aqueduct of Sylvius. *Left:* Antero-posterior view showing greater portion of cavity to the right. Note small cavity in septum pellucidum. *Right:* Lateral view showing roof of cavity of 6th ventricle.

FIG. 5. Posteroanterior view, showing the entire outline of cyst of 6th ventricle. (In this view the sac appears to have shifted more to left.)

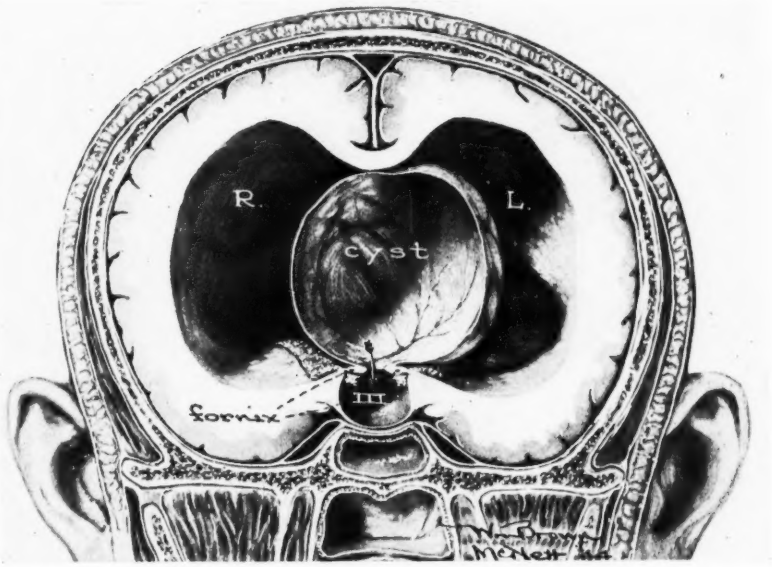

FIG. 6. Artist's conception of cyst as visualized by encephalogram and operation.

only slight evidence of separation, it was thought that the abnormality probably represented a cyst of the cavum Vergae.

Operation. A craniotomy was done on March 6, 1943 under avertin and ether anesthesia. A small osteoplastic flap was reflected in the right frontal area (Fig. 7). The cortex appeared normal but the gyri were slightly widened. The cerebrum was incised and the lateral ventricle entered. A midline, bluish-white mass, about the size of a gallbladder, could be seen bulging into the lateral ventricle and compressing the foramen of Monro anteriorly. The mass was displaced laterally in order to visualize its attachment at the base. Small, hair-like blood vessels at the neck of the sac were closed with silver clips and cautery, and the sac incised. Immediately following incision there was a copious flow of clear fluid and the sac collapsed. It was resected at its base, leaving a small portion which was attached to both sides of the roof of the third ventricle. The choroid plexus in the right lateral ventricle was then obliterated by electro-cautery (Fig. 8). The ventricle was filled with normal saline, the dura was closed and the osteoplastic flap replaced.

Course. The patient did well following operation except for a transitory period of irritability. Reexamination by Dr. Silverstein on March 24, 1943 (18 days postoperatively) showed the following: "The child is cooperative. There is no evidence of a mental defect. There are no abnormal behavior changes. Irritability and other personality disturbances, which appeared following operation, have disappeared. Neurologically, the findings are negative except for a suggestion of a slight spasticity in the right lower extremity and a Babinski sign on the left."

Psychometric examination (two weeks following operation) revealed no change in mental age.

Pathological Examination. Dr. W. L. C. Spaeth's report on the tissue removed at operation was as follows: "Specimen consists of a parchment-like tissue representing the sac of a cyst, the contents of which have been evacuated. The cyst measures 5 cm. in diameter. Running from the base a few fine, hair-like vessels can be seen" (Fig. 9).

Dr. Helena Riggs, Neuropathologist to the Philadelphia General Hospital, described the histopathology of the cyst wall as follows: "The wall consists of two distinct layers: a meso-

dermic, composed of collagen bands and one made up of a feltwork of fibres of ectodermal origin. The collagen layer comprises bands of fine, wavy, acellular fibres separated by what

FIG. 7. Patient, five days post-operatively, before sutures were removed. Incision in frontal area.

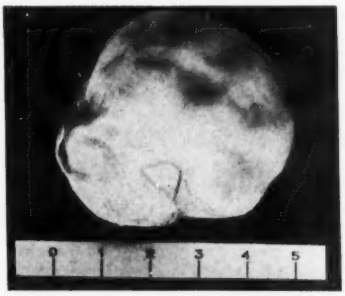

FIG. 9. Cyst of 6th ventricle removed at operation. Sac was translucent *in situ* and appears opaque because it was fixed in formalin and filled with cotton to keep its shape. Note hair-like vessels at base of sac.

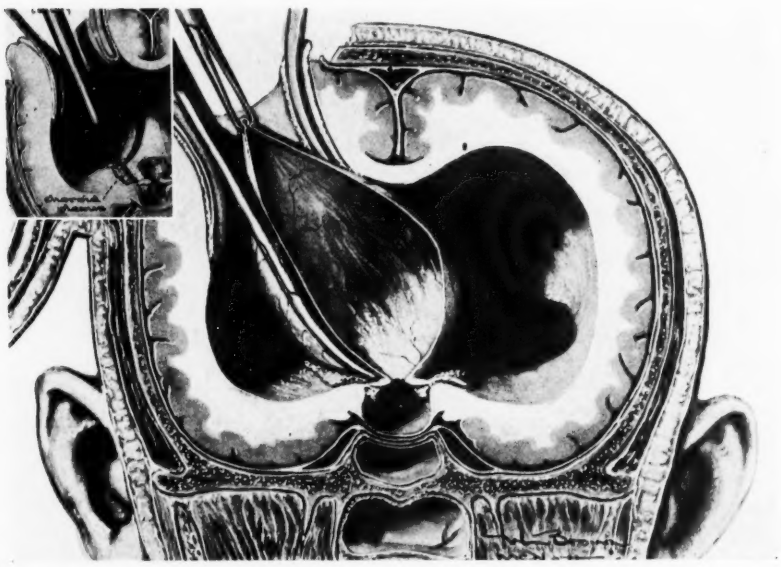

FIG. 8. Small, osteoplastic flap reflected in frontal area, cerebrum incised, cyst mobilized into lateral ventricle and resected at its base, and choroid plexus of lateral ventricle coagulated.

appear to be fluid spaces. In some areas these bands invade the ectodermal layer and even surround it. Only occasional cells are seen in this layer, lying parallel to the collagen fibres and consisting of an elongated cell body with a long, slender process at either pole. The layer of loosely interlacing fibres runs at right angles to the collagen bands. The free border is outlined

by a single row of flattened ependymal-like cells (Fig. 10), but in many places this layer is eroded and the fibres project into the cavity of the cyst. Cells resembling neuroblasts and primitive spongioblasts are scattered between the fibres; the severe degenerative changes present, however, prevent absolute identification. Many of them are triangular in shape, with a thick, elongated process continuous with the apex of the cell body. In some, both a nucleus and a prominent nucleolus are present. Multipolar and forms resembling primitive neuro-

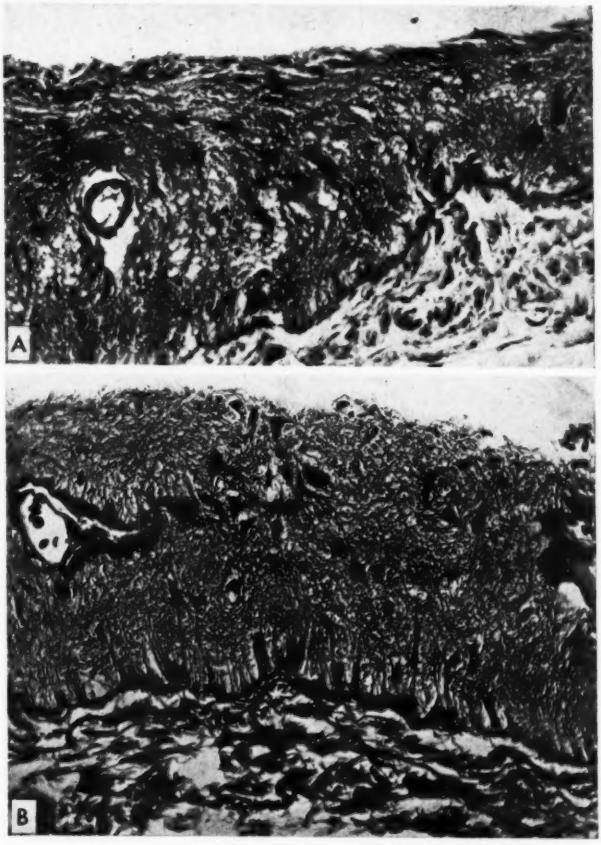

FIG. 10. Wall of cyst removed at operation (see text). Trichrome, ×414.

blasts, are also noted. Occasionally, cells resembling ependymal spongioblasts are seen at the margin of the two layers (Fig. 10B).

"The neural layer of the cyst shows large blood spaces containing red blood cells at relatively regular intervals. These consist of a comparatively thick wall of collagen fibres and a layer of endothelial cells. The vessels are surrounded by a dilated perivascular space, outlined by a rim of collagen fibres. No other vascular structures could be found and the mesodermic layer appears relatively avascular. The close resemblance of the neural layer to the ependymal cell plate as described by Globus and Kuhlenbeck[3] suggests that the cyst wall originates from the same analogue as the lining of the ventricular system."

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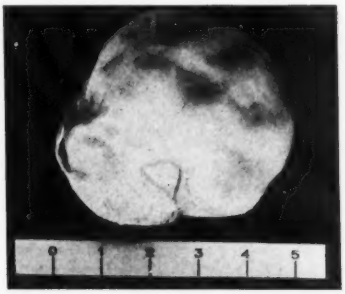

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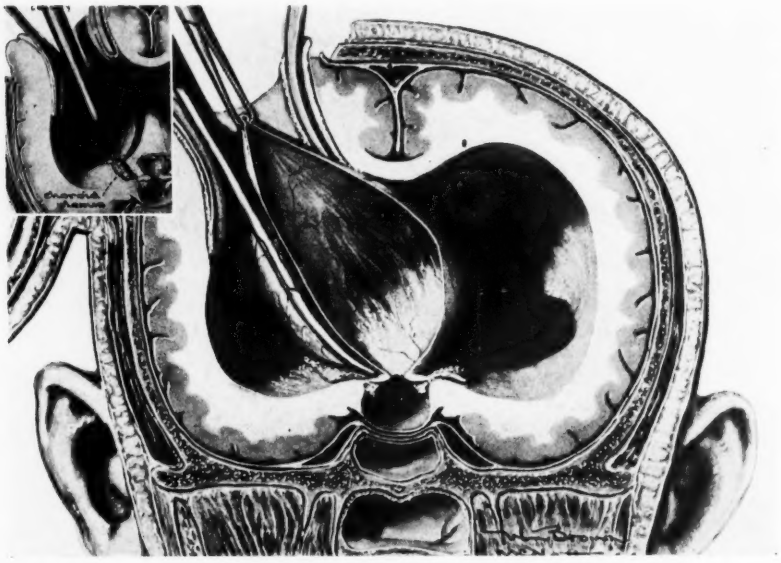

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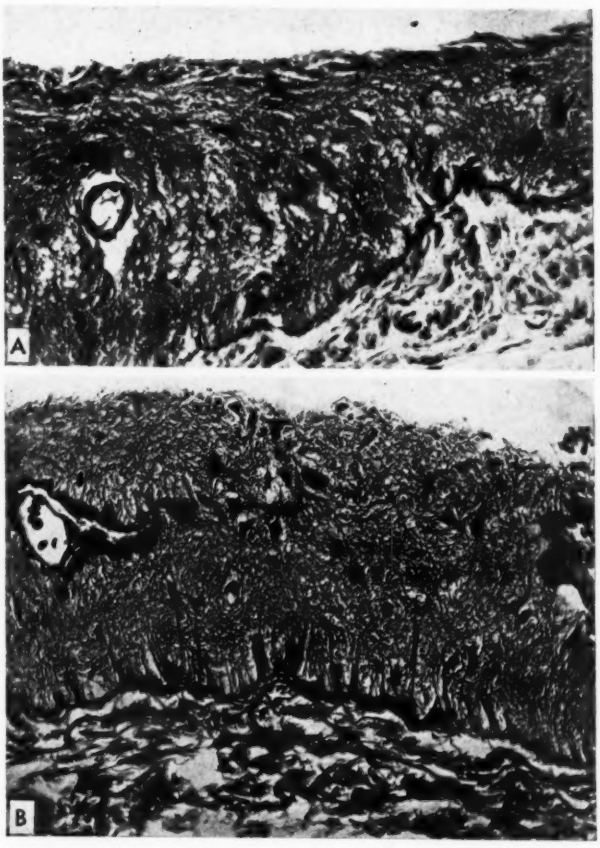

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Subsequent History. Reexamination of the patient, 1½ years after operation, revealed that she had had no convulsions, headaches had disappeared, circumference of the head remained unchanged and the neurological examination was negative. She took no medication and her school work had been satisfactory.

DISCUSSION

Symptomatology. There is no syndrome characteristic of a cyst of the 5th or 6th ventricle. These cavities may be slightly enlarged or dilated without intracranial symptoms. A cyst large enough to obstruct the foramen of Monro anteriorly and/or the aqueduct of Sylvius posteriorly, will cause symptoms of increased intracranial pressure. Obstruction in infancy results in a progressive hydrocephalus. If the cyst ruptures or communicates with the ventricular system, the symptoms may suddenly disappear or abate only to recur later if the cavity refills or proper emptying is prevented by the position of the cyst (see case report). Convulsions, at times unilateral, may occur. Frontal lobe symptoms may be present.

Roentgenographic Studies. Plain films may show direct or indirect evidence of increased intracranial pressure, but are not diagnostic. Encephalography or ventriculography (if choked disc is present) may show an air-filled cavity above the third ventricle extending into both lateral ventricles, if the cyst communicates with the ventricular system (Fig. 4). If the cyst does not communicate with the ventricles, a dense defect may be found extending into the mesial walls of both lateral ventricles and encroaching upon the superior surface of the third ventricle.

Treatment. Dandy approached the cyst through the corpus callosum and ruptured the wall of the cyst, producing a communication with the lateral ventricle. Van Wagenen and Aird suggested a transcortical approach through the lateral ventricle, with rupture of the cyst wall to establish a communication with the lateral ventricle. Love, Camp and Eaton used a transventricular approach with the removal of the cyst wall.

In the present case, a transcerebral and transventricular approach was used; the cyst sac was delivered into the lateral ventricle and resected at its base (Fig. 7). Although it appeared that resection of the sac would prevent further hydrocephalus, the choroid plexus was cauterized as an additional precaution because it was recently proven to the writer (case to be reported) that cauterization of one choroid plexus can, under certain conditions, stop a progressive hydrocephalus.

SUMMARY

A case is reported of a child, 6 years of age, who had a history of headaches, convulsions and enlargement of the head. The neurological examination gave no clue as to the site of the lesion. Encephalography showed a huge cyst of the cavum of Verga or the sixth ventricle. The cyst was removed through a transventricular approach and the choroid plexus in the lateral ventricle coagulated. The child has been free of headaches and convulsions

since operation and at present (one and a half years postoperatively) is attending school and shows no abnormality of mentality or personality.

It was Dandy's belief that the cavity was not a part of the ventricular system. His opinion was based on the shape, size and position of the openings in the cyst that communicate with the ventricle and not on any histopathological evidence. However, microscopic studies of the cyst wall of the case herein reported, suggest that the cavum of Verga may well originate from the embryonal ventricular system.

CONCLUSIONS

1) Small cysts of the 6th ventricle (ventricle of Verga) occur as normal, non-symptomatic findings in 2 to 3 per cent of all necropsies.

2) Large cysts obstructing the foramen of Monro or the aqueduct of Sylvius, produce latent, intermittent or persistent symptoms of increased intracranial pressure. Convulsions may occur. The neurological signs vary and there is no specific clinical syndrome.

3) Encephalography or ventriculography may prove diagnostic and show a circumscribed, globular mass between the enlarged lateral ventricle and above the third ventricle. This mass may or may not communicate with the third ventricle.

4) A transventricular approach with resection of the entire sac and cauterization of the choroid plexus, as done in this case, offers a method for complete removal of the cyst with control of the hydrocephalus.

5) The close resemblance in this case of the neural layer of the cyst wall to the ependymal cell plate as described by Globus and Kuhlenbeck suggests that the cyst wall originates from the same analogue as the lining of the ventricular system.

The writer expresses his thanks to Dr. Ernest Spiegel and Dr. E. E. Aegerter for their advice and suggestions.

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PERIPHERAL NERVE INJURY IN FRACTURES AND DISLOCATIONS OF LONG BONES*

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INJURIES of peripheral nerves in association with fractures and dislocations of long bones are frequent and the consulted literature includes many cases. The contributions of Bristow,[6] Speed,[20] Lewis,[11] Lewis and Miller,[12] Platt,[17] Stuck,[21] Watson-Jones,[23] and others consider the subject adequately. The present paper is a report on 51 patients operated upon for nerve injuries associated with fracture and dislocation of long bones. There were 53 such injuries in this series, more than one nerve having been involved in two cases. A portion of this work was reported in 1934.[10] This is not a statistical survey, since a majority of the patients were referred to the neurosurgeon as a last resort. However, a certain number among them were treated from the beginning with the orthopedic surgeon in charge. In the following few pages we propose to discuss this series and the lessons learned in their management.

Nerve injury associated with fracture and dislocation may be primary or secondary, as has been emphasized by almost all authors. The diagnosis of primary nerve injury is seldom made, and the physician treating the patient usually discovers the nerve complication several weeks after the injury, following the removal of a splint or a cast. In management the presence of a primary nerve injury is important. Secondary nerve injuries are attributed to scar and callous inclusion with eventual dysfunction of the nerve from pressure. A third type of nerve involvement, that is, a late neuritis or tardy neuritis, should also be defined for the sake of completeness. Tardy nerve involvement (usually ulnar) is associated with a latent period of many months or years, with eventual implication and dysfunction of the nerve.

MATERIAL

The 53 nerve injuries for which operations were performed included 32 radial, 9 ulnar, 3 median, 8 peroneal and 1 sciatic. The work was done mainly at the Receiving and Grace Hospitals in Detroit.

Radial Nerve Involvement. In Table I the radial nerve cases are analyzed. It is to be noted that there was radial dysfunction in association with fracture of the upper third, fracture of the middle third, fracture of the lower third, supracondylar fracture of the humerus and anterior dislocation of the head of the radius. The involvement was secondary in 19 and primary in 11 cases. The exploration was done under five weeks in 7 cases, from six to ten

* Presented before the Western Surgical Association, Chicago, Illinois, December 2, 1944.

weeks in 11, eleven weeks and over in the remaining 14. In 5 the radial nerve was found sectioned. In 3 of this group there was no operative procedure prior to the radial nerve exploration. In the other 2 an open reduction had been performed elsewhere and one could not ascertain whether or not the nerve involvement was primary or secondary (Fig. 6).

The results of exploration were gratifying in 26, unknown in 4 and poor in 2 cases. Of the two "failures," in one there was practically no radial nerve between the fracture site and the antecubital fossa, and in the other there was a gap of four inches of nerve loss. In the case of radial paralysis associated with fracture of the upper third of the humerus, the proximal and the distal ends of the nerve were dissected free through two incisions (Fig. 5); a lateral incision for the distal, and an incision on the medial aspect of the arm for the proximal ends. In this case the radial nerve had been incorporated in the healed fracture and the nerve was sectioned off the bone and sutured posterior to the humerus. Complete recovery ensued in fourteen months.

The usual incision for the exposure of the nerve in the supracondylar and middle third fractures of the humerus extended from the antecubital fossa laterally and posteriorly to the middle third of the arm. The nerve was dissected out in its normal position below and above the lesion, with further dissection at the site of pathological change. After freeing the nerve it was transposed into a live muscle bed. If the nerve had undergone neuromatous degeneration neurolysis was performed, and if the individual bundles, although swollen at the site of trauma, were still patent the nerve continuity was not disturbed (Fig. 4). If the nerve was found sectioned, it was sutured in the usual manner (Figs. 2 and 3).

We have had 4 instances of radial palsy associated with anterior dislocation of the head of the radius, with fracture of the ulna in 2 cases. These were treated by excision of the head of the radius, dissection of the nerve away from scar and its transposition into a muscle bed. An incision bisecting the antecubital fossa and extending toward the lateral aspect of the arm (Fig. 8) along the junction of the brachialis and brachio-radialis muscles was used. Recently the surgical exposure of the proximal end of the ulna and radius through one incision in Monteggia's fracture has been advocated by Boyd.[5] If such a fracture is complicated by radial paralysis, the open reduction and the inspection of the nerve may be carried out advantageously through two incisions: The posterior incision advocated by Boyd for the immobilization of the ulna, and an anterior incision bisecting the antecubital fossa to expose the radial nerve and the dislocated head of the radius. Reconstructive work on the head of the radius through the anterior incision would be somewhat simpler (Figs. 7 and 8).

The prognosis in radial paralysis is excellent. It is conceivable that in a certain number of our series, nerve function might have returned without operation, but early exploration in competent hands is justifiable and there is reason to believe that it decreases the total period of disability.[10] In most

TABLE I

Radial nerve injury associated with fracture or dislocation

Patient	Sex	Age	Year	Fracture or Dislocation	Primary or Secondary	Interval before Surgery	Operation	Result
J.R.	M	28	1930	Fractured humerus junction upper and middle thirds	Primary	14 weeks	Neurolysis and transposition	Recovery
C.J.	M	41	1930	Fractured humerus middle third	Secondary	6 weeks	Transposition	Recovery
E.M.	M	20	1930	Comminuted supracondylar. Previous open reduction	Secondary	7 weeks	Neurolysis and transposition	Recovery
C.S.	M	43	1930	Supracondylar	Secondary	10 weeks	Neurolysis and transposition	Recovery
S.T.	M	14	1930	Fractured ulna and dislocation head of radius	Secondary	4 weeks	Transposition	Recovery
J.R.	F	8	1931	Fractured humerus junction middle and lower thirds	Primary	13 weeks	Neurolysis and transposition	Recovery
S.H.	F	37	1931	Fractured humerus middle third	Secondary	13 weeks	Neurolysis and transposition	Recovery
J.M.	M	36	1931	Fractured humerus middle third	Secondary	11 weeks	Transposition	Recovery
J.G.	M	50	1931	Fractured humerus junction lower and middle thirds	Secondary	9 days	Neurolysis and transposition	Recovery
F.S.	M	56	1931	Fractured humerus lower third	Primary	5 weeks	Neurolysis and transposition	Recovery
J.C.	M	40	1932	Fractured humerus junction middle and lower thirds	Secondary	5 weeks	Neurolysis and transposition	Recovery
M.M.	M	50	1933	Dislocation of head of radius	Secondary	9 weeks	Neurolysis and transposition	Partial Recovery
J.G.	M	30	1934	Fractured humerus middle and upper third junction	Primary	20 weeks	Resection, neuroma. Nerve suture	Recovery
M.D.	F	40	1934	Fractured humerus middle third	Secondary	10 weeks	Transposition	Recovery
J.F.	M	41	1935	Fractured humerus middle third	Primary	17 days	Neurolysis and transposition	Unknown
H.B.	M	22	1936	Fractured humerus lower and middle third junction	?	8 months	Nerve suture	Recovery
E.S.	F	41	1936	Fractured humerus middle third	Primary	12 weeks	Neurolysis and transposition	Recovery
E.G.	F	55	1937	Fractured humerus lower third	Primary	5 months	Neurolysis	Recovery
P.M.	M	10	1937	Supracondylar	Primary	9 weeks	Neurolysis	Recovery
S.S.	M	20	1937	Fractured humerus junction middle and lower thirds	Secondary	5 weeks	Neurolysis and transposition	Unknown
M.K.	F	18	1937	Compound elbow	Primary	5½ months	Exploratory	Failure
H.P.	M	16	1938	Fractured humerus lower third	Secondary	12 weeks	Transposition	Recovery
M.M.	F	23	1938	Fractured humerus junction lower and middle thirds	Secondary	10 weeks	Transposition	Unknown
F.T.	M	38	1938	Anterior dislocation of head of radius	Secondary	9 weeks	Neurolysis and transposition	Recovery
P.M.	M	16	1939	Fractured humerus lower third	Secondary	6 weeks	Transposition	Recovery
P.C.	M	30	1940	Fractured humerus junction lower and middle thirds	Primary	7 months	Nerve suture	Recovery
J.K.	M	26	1940	Fractured humerus middle third	Secondary	9 weeks	Neurolysis and transposition	Unknown
M.F.	M	37	1940	Dislocated radius at elbow	Secondary	10 weeks	Transposition	Recovery
J.K.	M	19	1941	Comminuted humerus lower third	?	4 months	Suture impossible	No improvement
O.H.	F	43	1942	Fractured humerus middle third	Secondary	11 weeks	Transposition	Recovery
G.B.	M	30	1942	Comminuted humerus lower third	Primary	6 days	Transposition	Recovery 4 months
G.B.	M	34	1944	Fractured humerus middle third	Secondary	12 weeks	Transposition	Recovery

cases, beginning return of function is heralded by voluntary contraction of the brachio-radialis muscle. Two to four months later complete return of function to the extensors of the wrist and hand ensued. During convalescence the usual cock-up splint is used. When the nerve is not found lacerated the prognosis is usually excellent. In the majority of cases in our series complete return of function was obtained three to six months after exploration.

It may be noted from Table I that there were many more examples of radial palsy in 1930 and 1931. This is in direct ratio to the manipulative treatment these patients received. From 1932 on very few patients were manipulated, and the number of radial paralyses definitely decreased.

Ulnar Nerve Involvement. The ulnar nerve (Table II) was involved in nine cases. It was thought that the nerve lesion was primary in 7 and secondary in 2. Three patients with internal condylar fracture were operated on five weeks, six weeks and three months after the injury respectively (Fig. 10). In 2 cases, compound fracture of the ulna with ulnar nerve involvement was repaired immediately (Fig. 12). The ulnar neuritis associated with fracture of the upper third of the humerus was treated six months after the accident (Fig. 9). One patient with nerve involvement associated with fracture of the lower third of the humerus was operated upon seven months after injury. In the case of ulnar neuritis associated with fracture of the middle third of the ulna and radius repair was made five and a half months after injury. The patient with fracture of the middle third of the ulna was operated upon four months after trauma. In the latter, the nerve was found partially sectioned (Fig. 11). The ulnar nerve was transposed and in almost every instance a neurolysis was performed. In ulnar neuritis with fracture of the internal condyle of the humerus the nerve was transposed to the anterior aspect of the elbow.

Median Nerve Involvement. The median nerve (Table II) was found involved in 3. In 1 there was a bullet wound with supracondylar fracture of the humerus. The bullet was found almost imbedded in the nerve and its removal, followed by neurolysis, resulted in return of sensation to the median distribution of the hand in a matter of weeks. The other 2 were associated with dislocation of the elbow. In 1, the nerve was actually in the elbow joint and was freed five and one-half months after the injury (Figs. 13 and 14). In the other, the nerve was found in a bed of dense scar from which it was freed and transposed (Figs. 15 and 16).

The results were satisfactory in 1, and in the remaining 2 there was evidence of improvement during the period of follow-up.

Peroneal Nerve Involvement. The peroneal nerve (Table II) was involved in 8 in this series. The lesion was thought to be primary in 6 and secondary in 2. In 5 the nerve had not been torn at the time of trauma. A neuroma-like enlargement just above and behind the head of the fibula was present in 4 of these cases (Fig. 17), and in 1 the nerve looked flattened at operation for open reduction of fracture of the tibia and fibula at the knee joint. In 3, the peroneal nerve was found sectioned. These were operated on nine weeks, four and one-half months, and one year after the accident respectively. As shown

in Fig. 18, in the case explored one year after the accident there was extensive neuromatous degeneration involving about six inches of the distal end of the proximal portion of the nerve. In the case treated nine weeks after the accident there was so much nerve damage that a graft obtained from the sural cutaneous nerve was used. No recovery was noted at the end of eighteen months. In the third case, the lacerated peroneal nerve was repaired with ease. At the end of ten months there has been no evidence of recovery.

Where the nerve was not found sectioned, with or without neuromatous enlargement, the prognosis was usually excellent. In the cases of laceration no attempt was made at suture in one, in another a graft was used which was not successful, and in the third no evidences of regeneration have taken place at the end of ten months.

In adduction injuries of the knee with primary peroneal nerve paralysis the likelihood of nerve laceration is great. This is particularly true if there is a fracture of the proximal end of the fibula. Laceration of the external ligament of the knee frequently accompanies such injuries. The skin overlying the knee is intact. Early exploration is justifiable since the problem of nerve suture is much simpler soon after trauma.

Sciatic Nerve Involvement. In the single case of sciatic nerve involvement (Table II) there was posterior and upward dislocation of the femoral head with comminution of the acetabular margin. No improvement was noted, although the dislocation had been reduced adequately by operation. The sciatic nerve was explored twelve weeks after injury. Through an inverted hockey-stick incision on the posterior aspect of the upper third of the thigh, the nerve was dissected out as it emerged from the sciatic notch and extended on the posterior aspect of the gemelli muscles, between the ischial tuberosity and the greater trochanter. It was flattened and seemed to bulge posteriorly under some tension. It was transposed, utilizing the gluteal muscles. Return of function in this case was noted four months after operation with recovery in the tibial function only at the end of twenty-four months.

Multiple Nerve Injuries. In 2 cases in our series there was injury to more than one nerve. In one (C.J.) with fracture of the middle third of the humerus due to bullet wound, there was radial and median paralysis. Both nerves were explored six weeks after injury, the radial through an anterior lateral incision just above the elbow, and the median through an incision on the medial aspect of the upper third of the arm. In the other case (E.G.) there was radial and ulnar nerve involvement due to supracondylar fracture. The radial was explored five months and the ulnar seven months after the injury.

DISCUSSION

A review of the literature reveals that nerve injury associated with fractures and dislocations of long bones is frequent. It is quite likely that more instances would have been uncovered if a careful neurological examination were carried out in each case of fracture. Nerve involvement does not always

TABLE II

Nerve injury associated with fracture or dislocation

Patient	Sex	Age	Year	Fracture or Dislocation	Primary or Secondary	Interval before Surgery	Operation	Result
Ulnar nerve								
T.Z.	M	10	1933	Fractured ulna middle third	Primary	4 months	Neurolysis, partial nerve suture	Recovery
A.Z.	M	45	1934	Anterior dislocation of ulna, fractured lower third radius	Primary	Same day	Release of nerve from end of ulna	Recovery
B.B.	M	9	1935	Avulsion medial epicondyle of humerus	Primary	5 weeks	Neurolysis and transposition	Recovery
W.H.	M	36	1936	Fractured trochlea and internal condyle	Secondary	6 weeks	Neurolysis and transposition	Improved
J.G.	M	20	1936	Fractured ulna junction upper and middle thirds	Primary	Same day	Nerve suture	Unknown
E.G.	F	55	1937	Fractured humerus comminuted lower and middle thirds	Primary	7 months	Neurolysis	Recovery
L.S.	M	23	1938	Fractured radius and ulna junction upper and middle thirds	Secondary	5½ months	Transposition	Marked improvement 9 months
J.S.	M	37	1939	Fracture of the upper third of the humerus	Primary	6 months	Neurolysis	Recovery in 1½ yrs.
J.W.	M	8	1940	Fractured medial condyle	Primary	3 months	Neurolysis and transposition	Recovery
Median nerve								
C.J.	M	41	1930	Compound humerus	Secondary	6 weeks	Neurolysis	Recovery
J.P.	F	7	1940	Dislocation at elbow	Secondary	5½ months	Neurolysis and transposition	Progress satisfactory at 3½ mos.
E.M.	M	41	1944	Dislocation at elbow	Secondary	6 weeks	Neurolysis and transposition	Progress satisfactory at 5 mos.
Peroneal nerve								
A.C.	M	58	1930	Compound fracture of tibia and fibula	Secondary	6 months	Neurolysis and transposition	No improvement 1½ yrs.
J.K.	M	44	1931	Fractured tibia and fibula	Secondary	9 weeks	Neuroma resected. Nerve suture with graft.	No improvement 1½ yrs.
G.T.	M	37	1931	Fractured tibia	Primary	5 weeks	Transposition	Recovery
A.G.	M	38	1934	Fractured fibula	Primary	3½ months	Neurolysis and transposition	Recovery 9 mos.
T.L.	M	26	1942	Adduction injury of knee	Primary	10 months	Neurolysis and transposition	Recovery 6 mos.
F.G.	M	42	1943	Open reduction for tibia and fibula	Primary	6 weeks	Exploration and transposition	Recovery
J.F.	M	23	1944	Dislocation knee joint. Fractured fibula	Primary	1 year	Exploration	No improvement
M.W.	F	17	1944	Fractured fibula	Primary	4½ months	Nerve suture	No improvement 9 mos.
Sciatic nerve								
H.M.	F	20	1942	Fractured acetabulum. Dislocated femoral head	Primary	12 weeks	Transposition	Partial recovery

need surgical intervention since in certain regions of the body conservative treatment of nerve injury with fractures and dislocations is successful.

The nerve may be injured by stretching; it may be contused or lacerated

at the time of trauma, or during manipulation. In the more chronic cases there may be scarring about the nerve and adhesions to the bone. Such a constriction of the nerve may cause neuromatous degeneration at the site of the lesion and eventual atrophy of the nerve distal to the region of pathological condition. The nerve may be caught between fragments with healing of bone about it.

In dislocations of the shoulder joint the axillary nerve and the lower portions of the brachial plexus may be involved. There is no evidence that opera-

TABLE III

Interval between injury and surgery

Nerve	0–5 weeks	6–10 weeks	11–15 weeks	16–20 weeks	20 weeks and over
Radial	7	11	8	2	4
Ulnar	3	1	1	1	3
Median		2			1
Peroneal	1	3	1	1	2
Sciatic			1		
TOTAL	11	17	11	4	10

TABLE IV

Results in 53 cases of nerve injury

Nerve	No.	Per cent	Recovered	Improved	No Improvement	Unknown
Radial	32	60.4	25	1	2	4
Ulnar	9	17.0	6	2		1
Median	3	5.7	1	2		
Peroneal	8	15.1	4		4	
Sciatic	1	1.8	1			
TOTAL	53		37	5	6	5

tive treatment of such complications is any more successful than conservative management.[17]

Fractures and dislocations about the elbow may be associated with nerve injury, and in selected cases early operative treatment is desirable. Fracture of the medial epicondyle may implicate the ulnar nerve. Fracture of the lateral condyle in childhood is the frequent cause of late ulnar neuritis. Supracondylar fracture caused median and ulnar nerve involvement in 15 per cent of the cases.[23] In our own series, the median nerve was found in the elbow joint in one case following a reduction of a dislocation.

The problem of nerve injury at the wrist joint is discussed by Abbott and Saunders,[1] who find that the median may be involved from acute palmar flexion of the wrist in the treatment of Colles's fracture. According to Watson-Jones,[22] carpal lunate dislocation, anteriorly, is a frequent cause of median dysfunction at the wrist.

Injuries about the hip joint are seldom associated with nerve involve-

ment except when the sciatic trunk loops around the neck of the femur in dislocation or during manipulation in reduction. In 1 case in this series there was involvement of the sciatic nerve with fracture of the pelvis, and posterior and upward dislocation of the head of the femur. Injuries at the knee joint present a serious problem as concerns primary peroneal nerve damage. Rupture of the peroneal nerve has been seen by many clinicians,[17,19,23] and early operative intervention in primary peroneal nerve involvement seems justifiable in adduction injuries of the knee joint.

The radial is the most commonly involved nerve in almost every series. Lewis[11] gives a percentage of 57.6 for radial involvement. In the group reported here the percentage is 60.4. In general the management of radial nerve palsy complicating fracture is different at different levels. In the middle third of the humerus radial nerve paralysis showing no improvement in eight to ten weeks should be treated by operation. In selected cases of primary nerve involvement earlier intervention may be indicated (Fig. 1). If an open reduction is contemplated, from the orthopedic standpoint of course, the nerve should be dissected clear of the fracture site and transposed into a muscle bed. In fracture of the upper third and the lower third, the period of watchful waiting could profitably be twelve to fourteen weeks before intervention.[4,10,17,23] In anterior dislocation of the head of the radius complicated by radial palsy, the head of the radius may be managed through an anterior approach and at the same time the nerve may be inspected and treated, if there have been no evidences of return of nerve function for eight to ten weeks. In Monteggia fracture complicated by radial palsy, if early open reduction is contemplated, the ulna can be immobilized through Boyd's incision and the radial nerve and the head of the radius may be exposed through an anterior incision bisecting the antecubital fossa and extending laterally toward the arm.

The ulnar nerve may be injured at various levels in the upper limb. Lewis[11] states that the ulnar nerve constitutes 25.4 per cent of peripheral nerve injury associated with fractures. In fractures of the medial epicondyle, a primary nerve involvement can be treated early to advantage with transposition of the nerve to the anterior aspect of the elbow.[2,3,15,17,18] In ulnar nerve involvement in the arm or forearm, a waiting period of three to four months before exploration is justifiable except where treatment by open reduction is better, based upon the circumstances of the case. Then the nerve should also be explored and treated accordingly.

In Lewis' series[11] the median nerve involvement constituted 5 per cent. The median nerve has been known to have suffered injury in fractures of the humerus,[6,11,20] dislocation of the elbow joint and at the wrist.[1,13,23] In our own group there was median nerve involvement in 2 cases of dislocation of the elbow. Early exploration following a reduction of dislocated elbow joint with signs of median involvement is proper. In other places the nerve may be explored in the absence of evidences of recovery in three to four months after the injury.

The management at the time of operation depends upon the type and ex-

tent of the nerve lesion. If lacerated, it is sutured in the usual manner. If partially lacerated, the uncut portion is carefully separated and the cut portion sutured. End-to-end suture is the best method for clinical results in the human,[19] although encouraging results are reported in the use of experimental grafts by Davis *et al.*[9] In the presence of a neuromatous enlargement at the site of adhesions between nerve and bone, a neurolysis is in order. If the nerve bundles are found to course through the neuromatous portion, even though somewhat swollen, longitudinal separation of the bundles is sufficient. In every case the nerve is transposed into a live muscle bed. At the elbow the ulnar nerve should always be transposed to the anterior aspect of the joint.

In compound fractures associated with soft tissue and nerve lacerations, immediate repair is proper in selected cases. In 2 in this series repair was undertaken a few hours after injury with good healing. With present-day therapeutic agents, early repair in such cases may be undertaken with greater confidence.

This discussion would not be complete without a few words concerning late or tardy neuritis, first described by Panas[16] and further elaborated by Broca,[7] Mouchet[14] and others. Almost always the involved nerve is the ulnar. A few instances of late median neuritis following Colles's fracture have been described by Abbott and Saunders.[1] We have seen an example of late neuritis of the sciatic nerve, due to gunshot wound, eleven years after injury. The explanation of tardy ulnar neuritis is as follows (Mouchet[14]): Injury, usually in childhood, to the lateral condyle with improper union eventuates in valgus deformity of the elbow. Several years later increasing tension on the nerve in its course through the epicondylar groove results in evidences of ulnar neuritis including sensory and motor phenomena and pain. That this is the pattern in a great many cases cannot be doubted. However, tardy ulnar neuritis from arthritic changes and minor injuries of the medial epicondyle neighborhood, with adhesion between nerve and surrounding tissues, is also possible. In these cases there may be eventual ulnar dysfunction from chronic irritation. Tardy ulnar neuritis has been considered in many papers[8] and its treatment by transposition of the nerve to the anterior aspect of the elbow and neurolysis is successful in the greatest majority of cases that come to operation early in the course of the ulnar dysfunction.

CONCLUSIONS

1. Early exploration in cases of nerve lesion associated with fracture of long bones is justifiable after complete study of the history, physical findings and X-ray films. If, from an orthopedic standpoint, open reduction is a procedure of choice, the involved nerve can also be explored at the same time.

2. Early exploration in ulnar nerve palsy associated with fracture of the medial condyle of the humerus is preferable. Anterior transposition of the nerve may then be carried out.

3. Early exploration of primary peroneal palsy is desirable in injuries of

the knee joint with fracture of the upper end of the fibula. There is a great likelihood of a torn nerve in most cases of primary peroneal palsy with fracture of the upper end of the fibula.

4. In fractures of the middle third of the humerus complicated with radial palsy, exploration in eight to ten weeks is justifiable if there are no evidences of returning function.

5. In compound fractures associated with nerve lesions, early repair is feasible, particularly with present day chemotherapeutic measures.

6. A nerve should be explored if there is no evidence of regeneration three to four months after a fracture of the neighboring bone.

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FIG. 1. Open reduction 6 days after accident in a case of supracondylar fracture and primary radial paralysis. Nerve found between fragments of bone. After reduction, the nerve was transposed into a muscle bed. Recovery in 5 months.

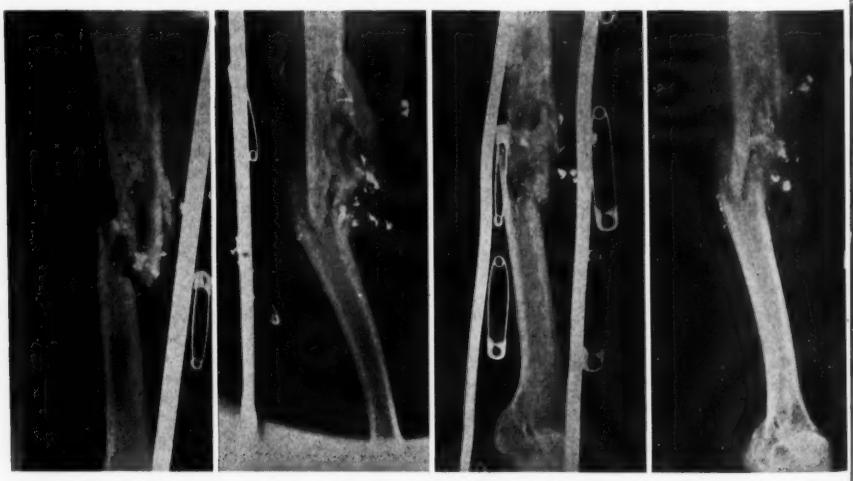

FIG. 2. Bullet wound of humerus with compound comminuted fracture and radial paralysis. At operation 7 months later, the nerve was found sectioned (see Fig. 3).

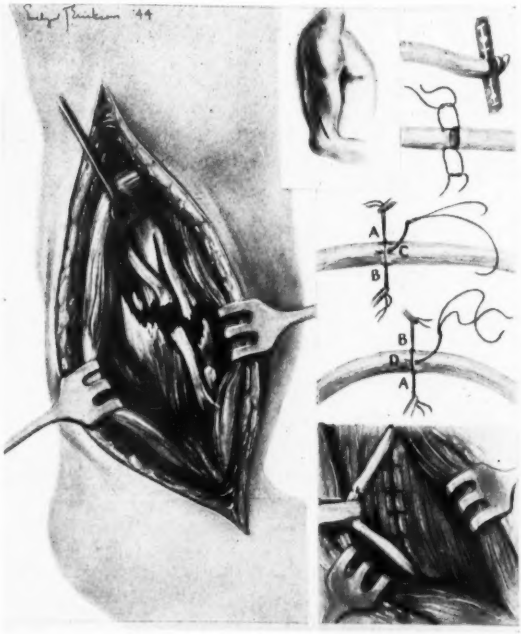

FIG. 3. Operative findings in Fig. 2. The lacerated nerve was sutured in the usual manner after the neuromatous ends were excised with a Gillette razor. Bone and nerve were then separated by interposing muscle.

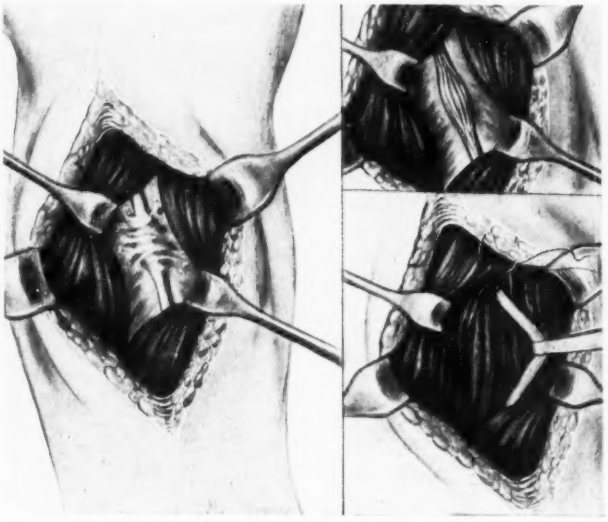

FIG. 4. Neuromatous degeneration in a case of radial palsy with fracture of middle third of humerus. Minimal callous formation at fracture site. Intervention 14 weeks after injury. Neurolysis revealed swollen patent bundles through area of pathological change. Recovery in 45 weeks.[10]

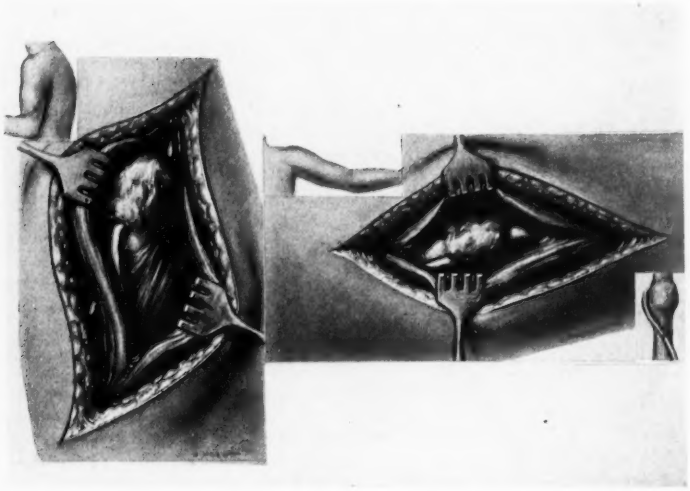

FIG. 5. Radial paralysis associated with fracture of upper third of humerus, explored 5 months after injury. Nerve found incorporated in the healed fracture. Lower end of nerve was exposed through a lateral incision and proximal end through an incision on medial aspect of arm and axilla. Nerve was sutured posterior to humerus. Recovery in 14 months.

FIG. 6. Radial nerve paralysis in a case in which a supracondylar fracture was treated by open reduction 3 months after injury. Six months after injury the radial nerve was explored and found sectioned. Nerve was sutured, with recovery at the end of 12 months. It could not be determined whether the nerve involvement was primary or secondary.

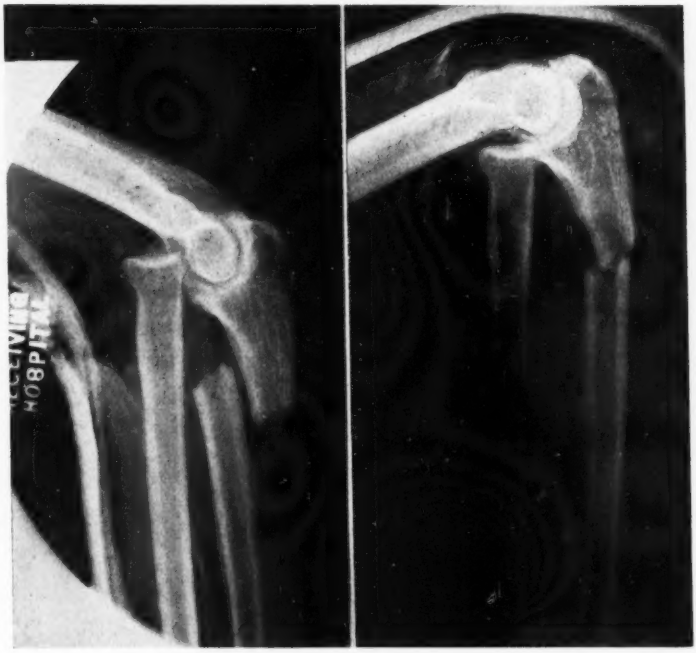

FIG. 7. Monteggia fracture complicated with radial paralysis. The radial head was removed and the nerve transposed through an anterior approach.

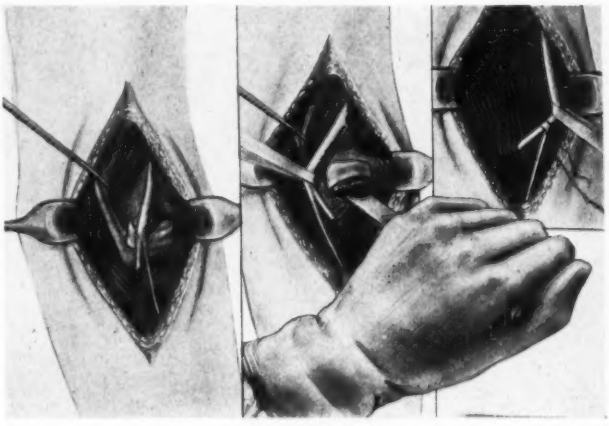

FIG. 8. Anterior dislocation of head of radius with fracture of upper third of ulna, associated with radial paralysis. Head of radius was removed 10 weeks after injury through an anterior approach.[10] Recovery.

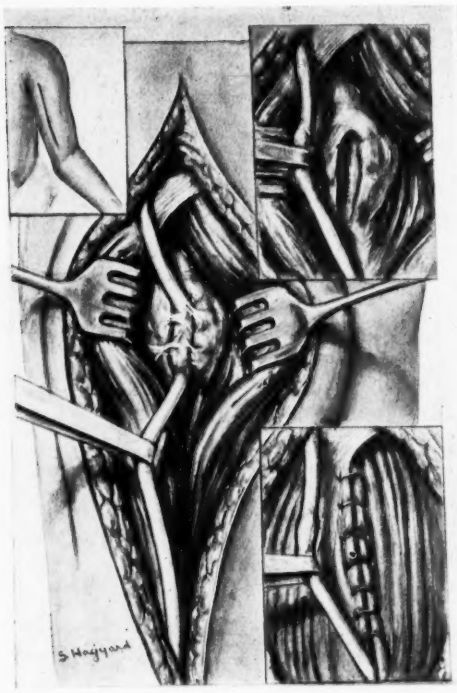

FIG. 9

FIG. 10

FIG. 9. Ulnar neuritis with fracture of upper third of humerus with adhesions of nerve and bone by scar. Exploration 5½ months after injury. Recovery in 18 months.

FIG. 10. Ulnar neuritis with fracture of medial condyle of humerus. Exploration 6 weeks after injury. Severe scar inclusion necessitating neurolysis. Nerve was transposed to anterior aspect of elbow. Return of sensation in 2 years.

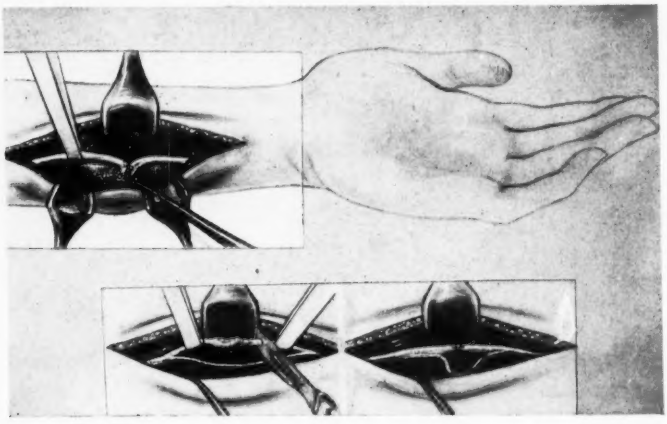

FIG. 11. Ulnar neuritis with fracture of ulna (junction of lower and middle thirds). Exploration 4 months after injury. Neuromatous degeneration at site of lesion. Neurolysis revealed a normal bundle easily separable from the remainder. Neuromatous portion resected and nerve sutured.

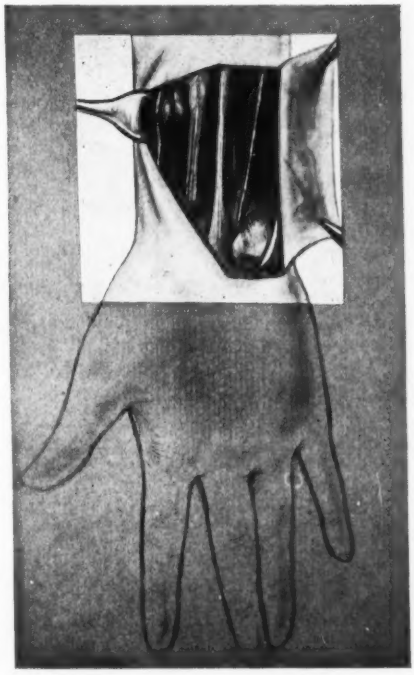

FIG. 12. Compound fracture dislocation of lower end of ulna, with ulnar nerve looping the articular surface. Immediate repair. Ulnar dysfunction in this case disappeared within a matter of days.

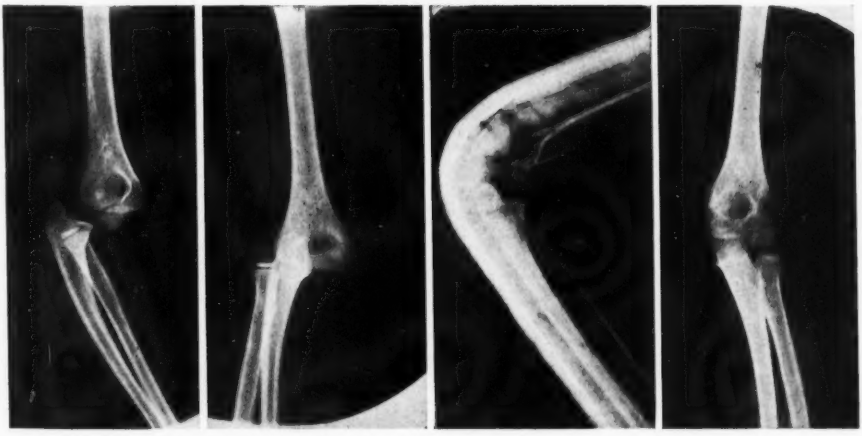

FIG. 13. Posterior dislocation of elbow joint successfully reduced. There was median nerve dysfunction and at operation 5½ months later the nerve was found traversing the elbow joint (see Fig. 14).

FIG. 14. Operative findings in a case of median nerve dysfunction following posterior dislocation of elbow joint. Nerve dissected proximal and distal to elbow joint. After removing a portion of the medial condyle, the median was liberated. It was flattened but appeared normal. Definite improvement in function ensued during a $3\frac{1}{2}$ months' follow-up. X-rays shown in Fig. 13.

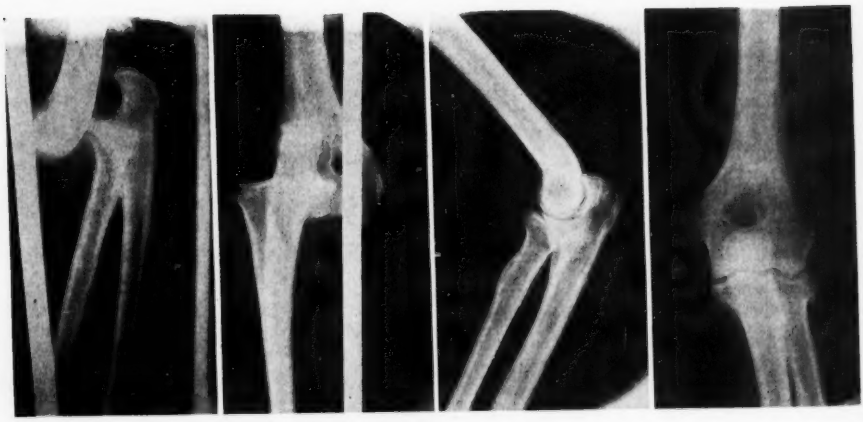

FIG. 15. Posterior dislocation of elbow joint, which was successfully reduced. This patient had median nerve involvement and was explored 6 weeks after injury. Nerve found in a bed of dense scar (see Fig. 16).

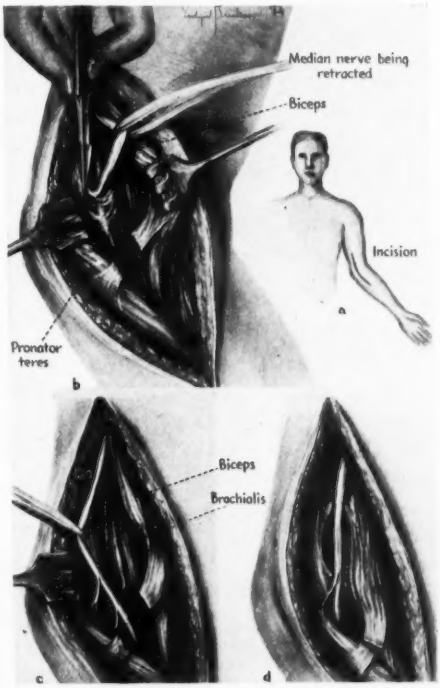

FIG. 16. Median nerve involvement in a case of dislocation of elbow joint. Nerve found bound down by adhesions but its structure looked normal. X-rays shown in Fig. 15. Improvement noted during a 5 months' follow-up.

FIG. 17. Neuromatous degeneration of peroneal nerve explored 4 months after accident. Neurolysis disclosed patent although swollen bundles through the neuroma. Recovery in 9 months.

FIG. 18. Extensive neuromatous degeneration of peroneal nerve following adduction injury of knee in a football accident. Exploration one year after injury. End-to-end suture was impossible.

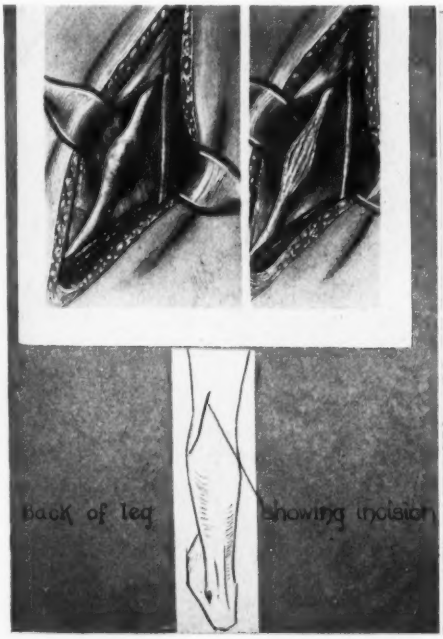

FIG. 17

FIG. 18

PANTOPAQUE MYELOGRAPHY: RESULTS, COMPARISON OF CONTRAST MEDIA, AND SPINAL FLUID REACTION

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RECENTLY a new contrast material, pantopaque, has been developed for myelography. Few detailed clinical reports are available. Spurling and Thompson[31] used it in 200 cases and found that it possessed the qualities of lipiodol and thorotrast, but, in contrast, small amounts were readily absorbed and it was easily removed. When removal was complete there were no sequelae. Partial withdrawal, however, was followed by about the same degree of irritation as after lipiodol. Ramsey, French and Strain[26] employed pantopaque in a series of 150 patients, 97 of which were operated upon. Diagnostic accuracy was found to be 95 per cent. The average estimated rate of absorption was 1 cc. per year. Copleman[9] also used this medium satisfactorily in 150 patients, and of these, 86 were explored; detailed results are not given. We have used pantopaque since September 1942. The first 300 cases form the basis of this report.

The chemistry, experimental findings, technic and methods for withdrawal have been adequately described elsewhere.[26,32,33] Check films are made following each myelogram and the amount of pantopaque retained estimated. It is usually possible to remove all but a few tenths of a cc. Probable factors accounting for incomplete removal are:

1. Inability of the patient to tolerate sufficient manipulation to remove the pantopaque. Discomfort is due to root pain produced by aspiration, etc.

2. Difficulty in adequately pooling the oil due to technical problems: tilting table, impingement of the arachnoid or nerve roots against the tip of the needle, etc. A small needle will add to the difficulty of aspiration.

3. Type of pathology present: arachnoiditis, diffuse tumor, or any lesion with partial obstruction, and consequent difficulty in movement of pantopaque with collection of it beneath the needle.

4. Extra-arachnoid injection.

In sixty-five cases, follow-up films were studied to determine the amount of absorption. This was done by measuring the quantity of oil originally removed. The size of the shadow of pantopaque (in subsequent x-rays), representing various amounts of remaining material, is quickly learned by experience. In seventeen cases, the average estimated absorption in one month was 0.2 cc.; in ten it was 0.4 cc. in two months; and in sixteen cases it was 0.5 cc. in three months. In the twenty-two remaining cases followed up to one year, the rate varied from 0.03 to 1 cc. Nine have shown absorption of from 1 to 1.5 cc. up to ten months. Maximum absorption of 1.5 cc. in two months was seen in a case in which 3 cc. were retained. From a detailed

study of our results it would appear that the largest amounts are absorbed in those in which the retention is the greatest, and *vice versa*, but the latter appears to vary from patient to patient.

Successive films show gradual fragmentation, movement and disappearance. In some cases the oil leaked through the puncture site into the subdural and even into extradural spaces. It has also extended some distance along the nerve roots. These situations in no way hinder the usual absorptive process and have caused no symptoms.

Encystment has not been seen. Experimental studies by Steinhausen *et al.*[32] have shown, however, that encystment may occur, particularly in the region of the cauda equina of dogs six weeks after injection. The reaction is considerably less than that noted after lipiodol and consists in a foreign-body response. Two clinico-pathological cases are included in their report. The spinal cord of one patient was examined seventeen days after injection. The pantopaque was still mobile and there were only a few polymorphonuclear leukocytes around the nerve roots. No encystment was noted. The second observation was made at laminectomy in the vicinity of extradural injection of the radiopaque substance nine days earlier. A degenerative reaction had occurred with infiltration by polymorphonuclear leukocytes, round cells and large monocytes.

In forty-eight cases of the present series, postoperative skull films were available to determine the incidence and effects of retained intracranial pantopaque (the longest time interval was one year). Thirty-four were negative and fourteen showed small amounts of oil in the basal cisterns. Only one of the latter resulted in symptoms and signs of meningeal irritation.

A 25-year-old pilot had a negative diagnostic spinogram on 6 September 1943 with incomplete removal of the oil. He was discharged on 9 September 1943, and almost immediately resumed flying. On 15 September 1943, following rather violent aerial maneuvers, he noted the onset of severe frontal headaches, nausea and vomiting, but continued on duty until hospitalized on 20 September 1943. Lumbar puncture relieved his symptoms and the cerebrospinal fluid showed 670 lymphocytes. X-rays disclosed small amounts of pantopaque in the basal cisterns. On 21 September 1943 blood studies revealed a leukocytosis of 14,750 with 73 per cent polymorphonuclear leukocytes, 16 per cent lymphocytes, 11 per cent monocytes; temperature was 100°F. Remaining and subsequent laboratory studies and vital signs were negative. Electroencephalogram on 29 September 1943 showed an abnormally patterned record with irregular wave forms consisting of mixed frequencies. Less synchronization was noted over the occipital regions. Overventilation increased the amount of interfering activity in all leads and caused slow wave formation. Repeat tracing on 7 December 1943 showed no essential change. Final examination on 5 May 1944 showed no neurological symptoms or signs, and all laboratory studies including electroencephalogram and lumbar puncture were negative.

Copleman[9] mentions nausea and vomiting in one case in which 1 cc. of pantopaque entered the cranial cavity following examination of the dorsal spine.

One other unexplained complication occurred in this series. Following routine removal of a typical "disc," bladder retention developed without other neurological findings. Subsequent pantopaque studies and operation revealed

an extensive arachnoiditis involving the cauda equina. In this patient, the pantopaque had been completely removed after remaining in the subarachnoid space for about 10 to 15 minutes, and it is difficult to presume that the arachnoiditis could have represented a reaction. Rather it would seem that there was some underlying neurological disorder, either coincidental or possibly precipitated by the use of pantopaque. The latter also does not appear consistent, as we have used the oil in numerous cases of arachnoiditis and degenerative cord lesions with no apparent change in the symptoms or signs.

VALUE OF CONTRAST MEDIA WITH PARTICULAR REFERENCE TO PANTOPAQUE

Due to the lack of a completely satisfactory contrast medium and improvement in clinical diagnostic methods, there has been a recent trend toward exploration for herniated nucleus pulposus on the basis of the clinical findings alone.[3,11,12,17,21,24,28,30] Relying entirely on this method, Bradford and Spurling[3] have been able to make a clinical diagnosis of ruptured disc in 80 to 90 per cent of the cases, and to accurately localize the lesion in 50 per cent. McKenzie and Botterell[21] found an error of only 15 per cent in distinguishing between ruptured discs at lumbar 4 and 5. Love and Walsh[20] recently wrote, "As our experience has increased, we have reached a point where we feel that our clinical diagnosis is just as accurate as the roentgenoscopic diagnosis obtained by the use of radiopaque oil, and more accurate than that obtained by the aid of air, which we now use almost routinely prior to operation." Shinners and Hamby[29] reported that, "All contrast studies were abandoned since it was realized that the results were not only confusing but often misleading." Dandy[11] especially is very emphatic in stating that, "All (media) are strongly contraindicated because they fail to disclose the small (concealed) disks, which are two-thirds of the total. Even spinal punctures contribute nothing and should be avoided." He feels the latter are of value only if a cord tumor is suspected, which has occurred in only one per cent of his cases. Therefore, he reasons it is needless to subject the remaining 99 per cent to useless procedures. In the diagnosis of discs Dandy,[11,12] has relied entirely on physical signs and symptoms, statistics (98 per cent occur at lumbar 4 and 5), narrowing of the intervertebral space on x-ray, mobility of the spinous processes at operation and exploration of two spaces if no disc is found. Eck[14] explores the space above the suspected level as well as the one below. Keegan[17] places considerable emphasis upon the careful determination of alterations in sensation in the diagnosis.

The individual objections to the use of contrast media will now be briefly discussed as they appertain to the various agents previously available and then in the light of the recent development of pantopaque.

There are several real disadvantages that limit the value of air and oxygen in intraspinal diagnosis: the density of these gases is poor and filling of the canal is often inadequate, making it difficult to demonstrate minimal nerve root lesions; considerable experience is necessary for interpretation

even under ideal circumstances; their application is usually limited to the lumbar canal unless a complete block is present. Moreover, immediate reactions are often severe. Perhaps the most valid criticism of all is the high incidence of positive findings at operation in those who have had normal pneumospinograms. Camp[5] found air to be 90 per cent accurate but 74 per cent of the negative cases later proved to have a lesion at operation. Hampton[15] found it satisfactory in only 50 per cent of the cases, whereas Poppen[25] claims verification at surgery in 85 per cent. Chamberlain and Young[7] further state that a lesion was found in every instance in which a positive x-ray diagnosis had been made in 300 cases. No actual statistics are given but in an earlier report[8] of 150 patients, only 10 lesions were verified at operation. Sanford and Doub[27] find air successful in only 35 per cent of the cases, but when injected into the epidural space the accuracy is 55 per cent. These authors claim that the latter method is ideal as reactions are not seen since the air does not enter the cranial cavity. Young and Scott[34] mention 13 instances in which the positive myelographic studies were later verified at surgery. Only five, however, represented herniation of the nucleus pulposus. Although the x-rays obtained following the two-needle technic described by Munro and Elkins[22] show improved visualization of the lumbar canal in many instances, the general objections to the use of air and oxygen already recorded are not altered.

Thorotrast has an accuracy of 93.7 per cent according to Nosik,[23] though there is an error of 11.1 per cent as proven by operation in cases that had been reported negative. Excellent visualization of the nerve roots has been demonstrated but the miscibility of thorotrast in spinal fluid limits its use to the lumbar region. There is always danger in the extra-arachnoid injection of a radio-active substance. Lastly, the necessity of subsequent forced spinal drainage entails several lumbar punctures and requires two to three hours for removal.

Immediate reactions following the use of tyrogel[18] are more severe than with other opaque media and constitute the chief objection to its use. These consist of headaches, nausea, vomiting, moderate pyrexia and a pleocytosis averaging 5,000 to 7,000 per c.mm. They usually subside within a week and no long-term sequelae have been noted in 44 cases (30 myelograms and 14 ventriculograms). It is said to be gradually absorbed and excreted by the kidneys within five to seven days. Further research on this substance has been suspended due to the war and it is not available for general use.

In spite of the excellent localizing value of lipiodol (Camp and Addington,[6] 96.8 per cent; Hampton,[15] 93 per cent), there have been numerous objections and disadvantages to its routine use. These include: difficulty in removal; very slow rate of absorption with subsequent possibility of encystment, nerve root irritation and medico-legal complications; and contraindication in presence of inflammatory and degenerative diseases. Myelograms may be negative in the presence of laterally placed protrusions of the nucleus pulposus and anatomical variations in the cul-de-sac. Eck[14] further points

out that lesions in the cervical and dorsal regions are poorly demonstrated and that the canal is filled only with difficulty. Finally, the most current objection is that a diagnosis may be made on the basis of clinical findings alone. Among those who emphasize this, however, some still use lipiodol to demonstrate a lesion in atypical or equivocal cases.

We have now had the opportunity of using pantopaque in 300 successive cases with excellent results. There were 150 patients operated upon for herniation of the nucleus pulposus and a lesion was found in 146 instances. Of the cases in which explorations were negative, myelography had shown suggested nerve root defects in two and an atypical deformity of the lumbar canal in one. Slight unilateral defects were seen in two additional patients; one of these presented a disc at another level, both on spinogram and subsequently at operation. Two operations were performed in which the pantopaque studies were considered negative; exploration revealed no abnormal

TABLE 1

Surgically verified cases of herniated nucleus pulposus.

X-ray classification	Authors' series (146 cases)		Camp and Addington (194 cases)	
Nerve root defects (enlargement and displacement)	72	49.3%	96	48.9%
Unilateral defects	53	36.3%	127	65.5%
Bilateral defects (18 removed from one side)	21	14.4%	67	34.5%
Partial obstruction	9	6.2%	22	11.3%
Complete obstruction	1	0.7%	5	2.6%
Multiple discs	16	10.9%	21*	10.8%

* In two of these 21 cases, involving L-4 and L-5, the second protrusion could not be visualized by X-ray.

findings. Excluding the latter two cases, therefore, pantopaque was found to have a localizing value of 96.7 per cent.

Multiple discs were removed in 16 instances. More than one lesion was present in four other cases, in which there was an interval in the appearance of the two discs. All herniated nuclei pulposi were found in the lumbar area (with one exception which was not included in this series), 94 per cent occurring at lumbar 4 and 5.

The x-rays of the patients operated upon were available for further study and these were classified as shown in Table 1. For statistical comparison, the figures obtained by Camp and Addington,[6] using lipiodol, have been included. Camp and Addington found a unilateral deformity of the canal the most common type of defect. In those cases in which the deformity of the protruded disc itself was slight, they gained additional evidence from a study of the nerve root shadows for signs of associated enlargement or displacement. In 96 of their 194 cases of disc defects, nerve defects were also present. This accounts for the apparent discrepancy in the figures for the two series

as recorded in Table 1. In our series nerve root defects alone were most often associated with the disc syndrome, there having been 72 examples.

Pantopaque has been shown to compare favorably with lipiodol in relation to x-ray interpretation and accuracy in confirming the lesion at operation. Moreover it is free from many of the undesirable qualities of lipiodol and appears to be the best contrast medium thus far available. Some investigators will undoubtedly object to the use of pantopaque, as they have previously objected to lipiodol, because of the possibility of an occasional negative spinogram in spite of a good history and positive physical findings. This occurs usually in the presence of laterally placed protrusions with compression of the nerve root in the intervertebral foramen in which there is no distortion of the normal configuration of the axillary pouch. It has also been observed when there were anomalies of the cul-de-sac, e.g., those with a narrow termination and others that end one or more segments higher than usual, occasionally above the lumbosacral junction. According to Dandy[11] two-thirds of the discs (concealed) are not demonstrated by myelography. We have had relatively few examples that would fit into the above category, and certainly this criticism would seem insufficient to entirely discard a procedure that generally has proved so satisfactory. Two such cases have been explored with negative findings. In several others operation was not performed, for administrative reasons. Encystment and nerve root irritation were not observed. Pantopaque has been used in degenerative and inflammatory conditions without deleterious reactions. Its use has been satisfactory in the dorsal and cervical regions, both as to filling and demonstration of defects.

The following facts further emphasize the value of contrast media and point out the marked possibility of error if too great reliance is placed on the clinical data and x-ray findings alone. We have been able to make a presumptive clinical diagnosis in 84 per cent of our cases and to place the lesion preoperatively in 60 per cent. These figures alone demonstrate the importance of a good contrast medium such as pantopaque, with which the lesion has been correctly localized in 96.7 per cent of our cases. Furthermore, Spurling and Thompson[31] recently reported that 40 per cent of the cases of ruptured disc can be demonstrated only by exploration or by satisfactory myelography. "While an exploratory operation may be a justifiable procedure, particularly if the operator is skilled in this type of surgery, we would prefer to use a simpler and more precise method." They further indicate that their experience with 200 pantopaque spinograms has been very satisfactory.

Some investigators rely on the reflex and sensory changes in the diagnosis of the exact level of the lesion. Dandy,[11] for example, states that in the presence of a diminished or absent ankle jerk the lesion in most cases will be found at lumbar 5. Discs at lumbar 4 rarely cause alteration in the Achilles reflex according to Echols.[13] Craig and Walsh[10] have shown in a series of 449 lumbar discs that the ankle jerk was altered in 68 per cent at lumbar 5, 37 per cent at lumbar 4 and 52 per cent at lumbar 3. The patellar reflex was diminished to absent in 49 per cent of the cases at lumbar 3, 20 per cent at

lumbar 4 and 9 per cent at lumbar 5. Sensory changes were most commonly noted over lumbar 5 and sacral 1, with little difference as to the site of the disc. Barr and Mixter[1] state that there are no reliable diagnostic factors that differentiate a lesion of the various discs. Bradford and Spurling[3] found the ankle jerk involved in 80 per cent of herniations at lumbar 5 and 25 per cent at lumbar 4. They further demonstrated that half of the lumbar discs cause some change in the Achilles reflex.

We have found changes in the ankle jerk in 85 per cent at lumbar 5, 61 per cent at lumbar 4, 66 per cent at lumbar 3 and 33 per cent at lumbar 2. Only occasionally has there been alteration in the knee jerk and this has occurred at any level. Sensory changes were most frequent in lumbar 5 and sacral 1–2 dermatomes, regardless of the level of the lesion. We feel that the size and relative position of the protrusion determine the neurological deficit more than the level of the lesion. For example, a small, laterally placed lesion may impinge upon only one root, whereas a larger or more medial lesion may involve several roots and hence give rise to more reflex and sensory changes.

Relying to a great extent upon dermatome hypalgesia, Keegan[17] has surgically verified a lesion in 78 cases. This means that changes in the sensory pattern were seen in 100 per cent of those operated upon. This is considerably higher than previously reported in larger series of cases where neurological examinations were carefully recorded, e.g. Love and Walsh,[20] 22 per cent; Bradford and Spurling,[3] 75 per cent; and 58 per cent in our experience. We have seen numerous instances of complete loss of ankle or knee jerks with no sensory changes demonstrable with ordinary tests and also at levels other than the first sacral and fourth lumbar nerve roots respectively, contrary to Keegan's[17] observations.

Our findings and those of others already mentioned clearly show that there is often considerable dermatomic and reflex disagreement with the actual level of the pathology. There are a number of factors that modify the interpretation of sensory disturbances: overlapping of dermatomic distribution, incomplete and intermittent nerve root pressure, multiple lesions, compression of more than one root in large herniations, and presence of functional element. One cannot depend entirely upon the type and radiation of pain in the diagnosis of discs above lumbar 4 as claimed by Dandy,[11,12] Keegan,[17] Echols,[13] and others.

Shinners and Hamby[29] recently reported a series of 100 spinograms performed with lipiodol, air and thorotrast with 20 false positives and 11 false negatives. It would appear that if one substance alone were used consistently over a period of time, one could better familiarize himself with the characteristic and possible types of asymmetries and would be less likely to err in interpreting contrast films.

Bell and Spurling[2] mention narrowing of the intervertebral space, occasionally, in the presence of discs but this is seen just as often in cases with no evidence of this syndrome. Love and Camp[19] found that lumbar 4 was fre-

quently narrowed when the rupture was elsewhere or when none at all was demonstrated. Hampton and Robinson[16] felt that narrowing of lumbar 5 interspace was of little localizing value but that at lumbar 4 it was helpful in 25 per cent of all cases or 33 per cent of lumbar 4 ruptures (24 cases). Bradford and Spurling[3] feel that in the presence of sclerosis of the adjacent vertebral bodies or localized hypertrophic arthritis, thinning of the fifth lumbar disc may be helpful, particularly when correlated with the clinical findings. Camp[4] mentions arthritic changes in 17 of 50 cases, only 5 of which, however, were localized at the site of the lesion. It has also been repeatedly demonstrated that narrowing of the lumbosacral disc is often on a congenital basis, particularly when associated with other anomalies. Our findings have conformed in all respects to those expressed above and emphasize that routine x-rays are not specific and may not be relied upon for diagnosis.

Other reasons demonstrating the value of contrast media are: (1) The possibility of multiple discs. (2) The fact that dorsal and cervical lesions may produce low back pain and sciatica. Camp and Addington[6] found that 31.8 per cent of the cervical tumors, 50 per cent of the tumors of the dorsal spine, and over 83 per cent of those in the lumbar area caused these symptoms. (3) The possibility of establishing an earlier diagnosis of intraspinal pathology before signs of compression appear. (4) The possibility of tumor, which may be multiple, arachnoiditis, etc. (5) The desirability of localizing the lesion so as to limit the amount of operative exposure and to shorten the actual length of the operation. (6) The fact that x-ray evidence of the lesion may be of definite medico-legal value. (7) To determine the cause of postoperative symptoms, such as recurrent or multiple discs, adhesions, etc.

CEREBROSPINAL FLUID STUDIES OF PATIENTS SUBMITTED TO PANTOPAQUE MYELOGRAPHY

In Series I, 20 patients were carefully investigated prior to myelography. This included physical and neurological examinations, complete blood studies, and the recording of the pulse, respiration, blood pressure and rectal temperature. The spinal fluid pressure was then measured in millimeters of water and a specimen completely analyzed.

Routine myelography was then carried out with the injection of 3 cc. of pantopaque in the lumbar subarachnoid space, as has been previously outlined.[26] All vital signs were then recorded every two hours for 24 hours, then every four hours for one week. Individual reactions were carefully observed from day to day. Lumbar puncture was performed on the first, second, third, fifth and seventh days following spinogram. On each occasion cerebrospinal fluid dynamics (mm. of water) were recorded and total protein and cells estimated. A white and differential blood count was made at the same time. The maximum normal spinal fluid cell count was set at 5, total protein, 45, and pressure, 190 mm. of water. For purposes of control, 5 patients were similarly studied without injection of pantopaque.

In Series II, comprising 40 additional cases, one lumbar puncture was performed prior to myelography with determination of total protein and cells. A second puncture was made at varying intervals following this procedure with repetition of the above tests. Many of these specimens were taken immediately prior to surgery, rather than through the exposed dura at operation, to avoid contamination with blood from the exposed field.

TABLE 2

Series I. Positive spinal fluid findings

Case	Amount of oil retained in cc.	Days after injection	Polys	Lymphs	Total protein	Pressure in mm. H_2O
1	0.6	2	3	1	20	210
		5	0	0	30	210
2	0.2	7	0	2	20	210
3	0.7	1	1	2	30	210
		3	0	0	30	240
4	0	3	0	9	40	50
5	0.6	2	3	3	10	130
6	0.5	2	2	6	50	192
		3	3	3	30	122
7	0.8	1	5	2	50	120
8	2.2	1	9	0	40	152
9	0.3	4	6	0	15	50
		7	6	0	15	50
10	0.6	1	8	1	125	120
		2	8	0	15	40
		3	26	0	150	50
		5	9	2	45	100
11	1.5	1	678	7	60	130
		2	67	3	30	150
12	1.0	1	18	3	30	90
		2	0	13	20	100
13	2.5	1	40	4	25	120
		2	22	12	40	120
14	2.8	2	40	5	5	96
		3	13	3	30	55
15	1.7	1	11	6	20	120
		3	6	4	30	190

The results of both series are recorded in Tables 2 and 3. Complete statistics are not given due to the extent of our studies and normalcy of much of our work. Five of the cases in Series I and the five controls showed essentially normal findings. One patient not included in these groups showed a marked local and general reaction following injection of pantopaque into a benign subcutaneous cyst of the lumbar region.

TABLE 3

Series II. Positive spinal fluid findings

Case	Prior to pantopaque			Days after injection	Post-pantopaque			Amount of oil retained in cc.
	Polys	Lymphs	Total protein		Polys	Lymphs	Total protein	
2	0	0	30	1	430	1720	125	1.5
3	0	0	30	1	0	0	50	0.8
4	3	5	25	1	4	9	40	1.5
7	0	0	50	2	2	3	80	2.0
9	0	0	30	2	2	17	50	0.5
10	3	2	100	2	6	5	50	2.0
13	0	7	30	3	1	6	55	2.5
24	0	0	20	12	0	4	70	1.2
27	0	0	60	29	1	0	160	0.5
28	0	0	42	30	0	670	25	2.5
31	1	2	30	55	4	1	125	0.1
32	0	0	30	67	7	14	30	1.5
34	1	2	10	83	1	1	60	3.0

SUMMARY OF SPINAL FLUID FINDINGS

Pantopaque produces a very slight transitory meningeal response following injection as determined from a carefully controlled study of 25 cases and an additional investigation of 40 patients. The spinal fluid changes are similar to but slightly less than those due to lipiodol. More severe variations are observed following air and tyrogel. Reactions following the subarachnoid injection of pantopaque vary in different individuals and are more common after incomplete removal. These are due to individual differences in tolerance to the oil and chemical condition of the material. The type of response consists in slight rise of the polymorphonuclear leukocytes and/or lymphocytes and occasional elevation of total protein and spinal fluid pressure. It is more common to see either a pleocytosis or elevated protein, although they may be associated. These changes occur most often in the first week, with the height of the variation from normal occurring during the first few days. In an occasional case there was an elevation of total protein or cells more than two months after injection of pantopaque. Symptoms of meningeal irritation may occur after an interval if pantopaque extends into the basal cisterns, as shown in Case 28. As a rule, however, actual meningeal signs and systemic reactions, which are not uncommon following injection of air and tyrogel, have not been seen. The spinal fluid has usually been clear and colorless throughout. There appears to be no direct relationship between the amount of pantopaque retained and the cerebrospinal fluid findings. The vital signs were unchanged with the exception of slight temperature elevation and leukocytosis in some instances. The presence of headache and increase in previous low back symptomatology was observed in all cases in Series I with or without the injection of pantopaque. However, these reactions were only occasion-

ally noted in Series II and after routine myelograms. It may be noted further that in some individuals an increase in cells in the spinal fluid and an elevation of temperature may occur following single or repeated lumbar punctures without the injection of an opaque medium. No new neurological signs developed following use of this substance, though such might be possible in the presence of a large obstructing lesion with precipitation of a block after injection. In that event, permanent sequelae could be avoided by immediate surgery. No gross pathological changes have been evident in cases where the subarachnoid space has been exposed at varying periods following spinogram. Finally, the use of pantopaque should be confined to the subarachnoid space.

CONCLUSIONS

We have presented our results following the use of pantopaque in 300 successive myelograms. Its accuracy in diagnosis was 96.7 per cent in 150 cases operated upon for herniated nucleus pulposus. In fluoroscopy and x-ray interpretation pantopaque is comparable to lipiodol, but it is unlike the latter in that it is easily removed, is gradually absorbed, reactions are extremely rare, it is not contraindicated in the presence of inflammatory or degenerative lesions, and it has not resulted in encystment. Further, the meningeal response to injection has been minimal and transient. Considerable evidence has been adduced to demonstrate the value of contrast media, with special reference to pantopaque, and in spite of the recent trend towards diagnosis of disc on the basis of clinical findings. Finally, we wish to emphasize that one should consider all available evidence in determining the presence of this lesion, viz., the history, clinical findings and pantopaque studies (including fluoroscopy and x-rays) rather than to rely on one factor alone.

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SUBEPENDYMOMA: A NEWLY RECOGNIZED TUMOR OF SUBEPENDYMAL DERIVATION

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This presentation was stimulated by a detailed study of a series of seven cases of brain tumors composed predominantly of ectodermal elements deriving from the subependymal glia. The purpose is to describe the characteristic histologic features of the tumor and to discuss its origin and its differentiation from other types of gliomas. Two cases will be described in detail; the salient facts concerning the others will be summarized in the general discussion.

CASE REPORTS

FIG. 1. Case 1. A large tumor arising from the floor of the IV ventricle and expanding toward the ventricular lumen.

Case 1. J.K., a 56-year-old man, was admitted to the hospital unconscious and in acute pulmonary edema. On previous admissions he had complained of repeated attacks of nausea, vomiting, rotatory vertigo, headaches and tinnitus. During the last ten years he had noticed a slowly progressing impairment of hearing. For several months prior to his final admission he complained about gradually increasing ataxic gait and he experienced difficulty in swallowing.

Examination on admission in 1938 disclosed a primary optic atrophy on the left and early papilledema with small hemorrhages on the right. There was a fine horizontal nystagmus on looking to either side, a slight weakness of the right facial nerve, and a moderate degree of atrophy of the right half of the tongue. The deep reflexes were hypoactive. No paralysis of the extremities and no sensory disturbances could be detected.

The cerebrospinal fluid was clear and was under 350 mm. of water pressure; it contained 4 lymphocytes and 83 mg. per 100 cc. of protein; the Wassermann reaction was negative.

On Jan. 31, 1938 a posterior fossa exploration was made. The operation disclosed a sessile tumor arising from the floor of the fourth ventricle. A specimen was taken for biopsy and a bony decompression was made. The dura was left open. His recovery was uneventful. He was about and active until a few days before his death on Dec. 25, 1943, 5 years and 11 months after the decompressive operation.

The pathologic findings exclusive of those of the nervous system were severe pulmonary edema, bronchopneumonia and acute left ventricular dilatation.

The significant brain findings are illustrated in Fig. 1. A large tumor, measuring 4.6 cm. in diameter and arising from the floor of the fourth ventricle, had completely filled out the greatly distended ventricular lumen. The sharply circumscribed tumor presented as a granulated grayish-brown irregular mass adherent to the floor of the fourth ventricle.

Microscopic examination revealed a moderately cellular and well vascularized neoplastic tissue whose two main constituents were readily distinguishable. There were small cells with a rim of ill-defined cytoplasm and a small light-staining oval or slightly elongated nucleus. These cells of ectodermal derivation formed irregular nest-like aggregations separated by large cords of fibrous tissue (Fig. 2). The latter elements represent the second important con-

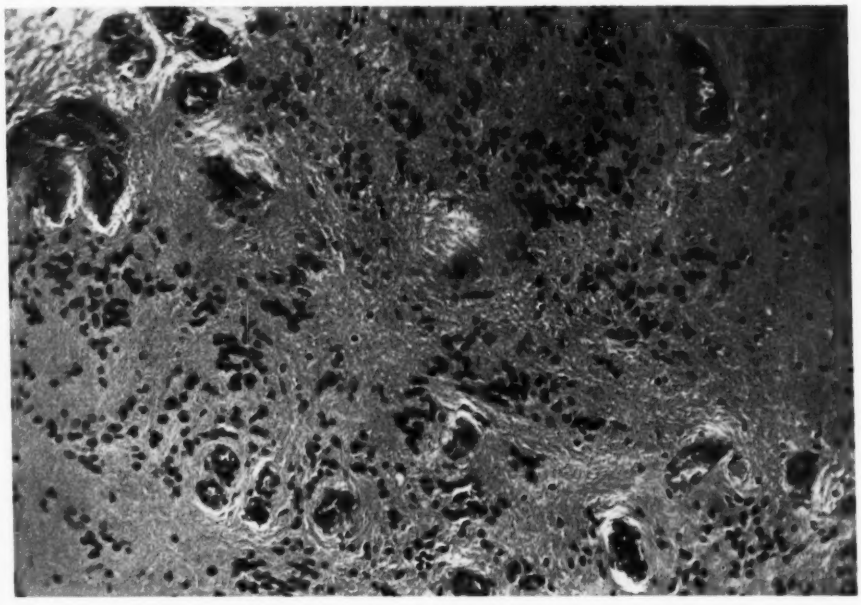

FIG. 2. Case 1. Irregular nest-like aggregations of mature glial cells separated by large cords of neuroglial fibers. Hematoxylin eosin stain (×165).

stituent of the tumor. The fibers appear to be arranged in broad streaming bundles running in various directions so that some are cut longitudinally and others in cross sections. The connective-tissue stroma was very scanty. With the van Gieson stain no collagen was seen. There was a small amount of connective tissue about the blood vessels but it did not penetrate into the tumor tissue proper; it was strictly confined to the vicinity of the vessels. With the silver stains a small number of bipolar cells could be differentiated; there was a single process which left each pole of the cell. Multipolar cells were rarely seen. No nerve fibers could be demonstrated. By means of phosphotungstic acid hematoxylin stain for glial fibers, a thick feltwork of neuroglial fibers could be seen. These appeared as long sweeping threads mostly arranged in bundles. Special stains, the cresyl violet stain and the Bodian silver impregnation method, demonstrated neither nerve cells nor nerve fibers. Mitotic figures and giant cells were absent.

The tumor appeared well demarcated from the surrounding tissue and was not invasive. At its base the tumor gradually blended through transitional cell forms with the normal ele-

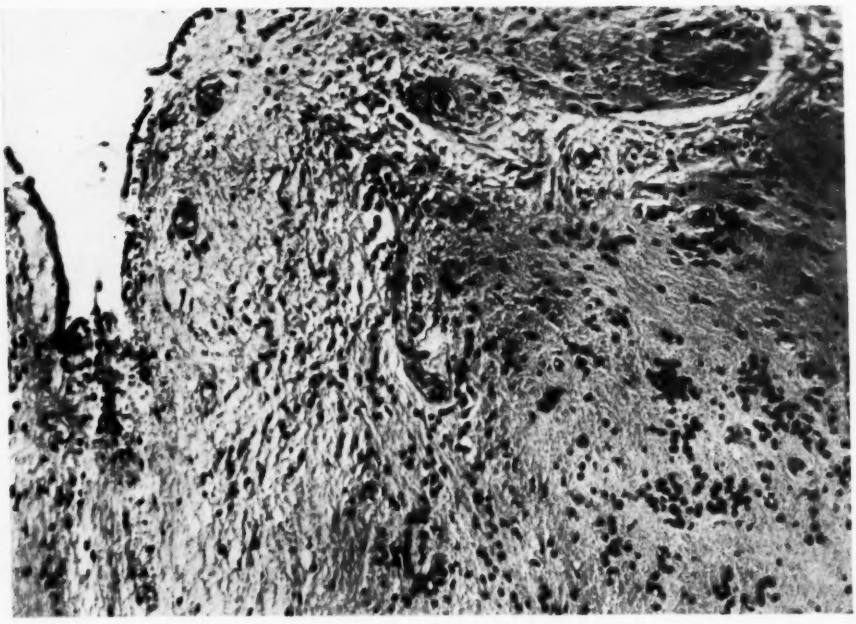

FIG. 3. Case 1. At the tumor base the neoplastic cells gradually blended through transitional cell forms with the normal elements of the subependymal glia. Note the similarity between the neoplastic cells and those of the normal subependymal glia. Hematoxylin eosin stain (×165).

ments of the subependymal glia (Fig. 3). The underlying gray substance of the floor of the fourth ventricle in the proximity of the neoplasm showed definite signs of compression and neuronal degeneration.

Case 2. C.K., a 53-year-old woman known to have arterial hypertension, was admitted to the hospital in an unconscious state. In the last few days prior to admission she complained of severe occipital headache and vomiting.

Examination on admission revealed a well developed obese unconscious white woman with right facial weakness and absence of all deep reflexes. There were signs of pulmonary edema and respiratory distress.

The cerebrospinal fluid was grossly bloody with an initial pressure of 200 mm. of water.

She expired on the day of admission.

Examination of the brain disclosed a slight fullness of the right cerebellar hemisphere and a diffuse bloody staining of the leptomeninges over both hemispheres. Horizontal sections through both lobes of the cerebellum revealed massive hemorrhage involving the white matter of the right cerebellar lobe and breaking through into the fourth ventricle. Sections through the medulla showed the presence of a small sharply outlined tumor nodule, arising from the floor of the fourth ventricle and measuring about one-half centimeter in diameter (Fig. 4). Coronal sections through the cerebral hemi-

FIG. 4. Case 2. Sharply outlined tumor nodule arising from the floor of the IV ventricle.

spheres revealed nothing abnormal except slight dilatation of the lateral ventricles. The blood vessels of the circle of Willis displayed advanced arteriosclerosis.

The microscopic appearance of the tumor was similar to that described in Case 1. Under low magnification the histologic structure of the tumor appeared fairly uniform. The predominant neoplastic elements consisted of rounded cuboidal or slightly elongated nuclei enveloped by a minimal amount of ill-defined cytoplasm. The cells formed aggregations separated by strands of fibrillary tissue (Fig. 5). Mitosis and giant cells were absent. Some areas of the tumor were composed almost entirely of a dense network of extremely thick neuroglial fibers arranged in large bundles.

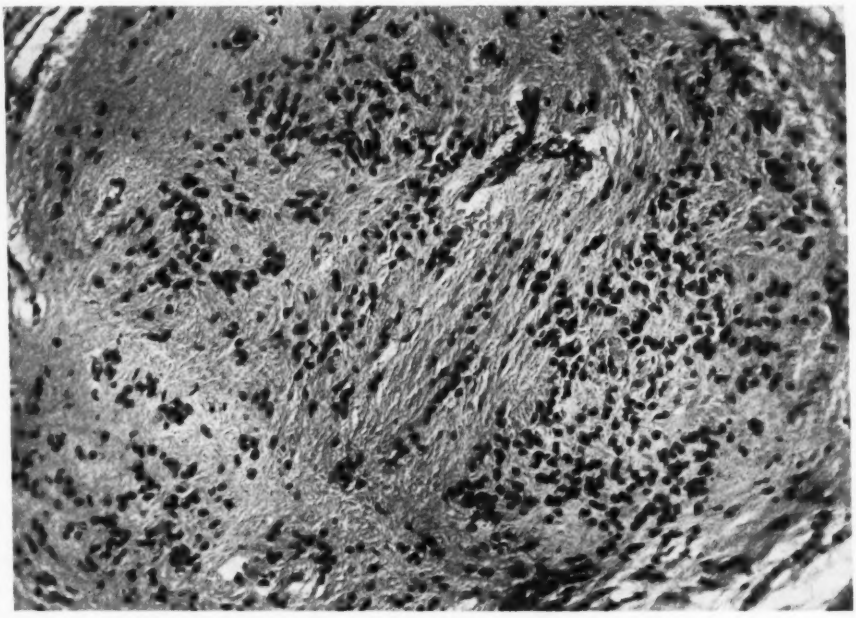

FIG. 5. Case 2. Aggregations of mature glial cells separated by strands of neuroglial fibers. Cresyl violet stain (×185).

Throughout the tumor there were numerous small blood vessels. In some regions, adjacent to the floor of the fourth ventricle, the subependymal glial cells and fibers were directly continuous with the tumor cells. By means of phosphotungstic acid hematoxylin stain for glial fibers, the large bands of fibrillary tissue separating the tumor cells were demonstrated as of neuroglial origin. Connective-tissue stroma was very scanty.

The tumor was well demarcated from the surrounding tissue, revealing an expansive compressive type of growth. At its base the tumor gradually blended through transitional cell forms with the normal elements of the subependymal glia. The floor of the fourth ventricle in the vicinity of the tumor showed ependymal granulations formed by thickening and proliferation of the subependymal glia, in appearance similar to that of the frankly neoplastic tissue. Sections taken from the right cerebellar hemisphere disclosed the characteristic picture of massive hemorrhage associated with vascular lesions typical of hypertensive brain disease.

GENERAL PATHOLOGIC ASPECTS

Gross Description. The tumors appeared slightly lobulated and were well demarcated from the surrounding tissue, thus revealing an expansive type of growth rather than an infiltrating one. The expansion usually has been directed toward the ventricular lumen, as illustrated in Fig. 1. At its base the tumor rarely extended beyond the ventricular floor (Fig. 3), but had a definite connection with the ependyma. The fresh cut surface was usually grayish-brown. Hemorrhagic or necrotic areas were uncommon.

Microscopic Description. From a study of all our material we may formulate a general conception of the histologic structure of a "subependymoma" as follows: In their major portions the tumors assumed in all cases a more or less uniform character. The cellular make-up exhibited a very strong resemblance to the normal structure of the subependymal glia. Under low power magnification the general structure of the tumor revealed a quite characteristic organization as illustrated in Figs. 2 and 4. Small clusters of glial cells without definite pattern and duplicating the subependymal glia were found side by side with interlacing bundles of neuroglial fibrillae.

Under higher magnification the cellular collections appeared to be composed of rather uniform cells. Most of the nuclei were of neuroglial type, ovoid or elongated in shape with scattered grains of chromatin. No mitotic figures were seen. Multinucleated cells were absent. The cytoplasm was very scanty and ill-defined. Some of the elongated cells showed rather short apical unipolar or bipolar processes with special staining methods such as Mallory's phosphotungstic acid hematoxylin. Small areas of greater cellular density alternated with larger areas of much lesser density. The latter were composed in larger part of strands of fibrillary tissue, which stained blue with Mallory's phosphotungstic acid hematoxylin stain and yellowish-brown with van Gieson and thus could be identified as neuroglia fibrillae. They usually appeared as long sweeping threads and were often arranged in bundles. Some of the fibrillae were thick and extended over several fields. A connective-tissue stroma was present in mild degree about the blood vessels only. No nerve fibers could be demonstrated.

In three cases there was a striking abundance of vascular channels: their walls were thin; they were occasionally surrounded by accumulations of extravasated red blood cells (Fig. 6).

In two instances there were large accumulations of calcium deposits within the tumor.

The margin of the tumor was in all cases fairly definite but there was never a capsule of connective tissue. The borders of the tumor always displayed an expansive compressing character of growth, rather than an infiltrating invasive one. The intimate connection of the tumor with the normal elements of the subependymal glia and its gradual blend through transitional cell forms with this particular portion of the ventricular wall were very striking.

THE HISTOGENESIS OF THE "SUBEPENDYMOMAS"

It is evident from the foregoing histopathologic data that the cases described, although they present a few minor differences, nevertheless belong to the same type of tumor for which the name "subependymoma" has been suggested. This term was chosen because it best describes the derivation of the tumor and indicates that its predominant cell type derives from the

FIG. 6. Numerous distended thin-walled vascular channels. Cresyl violet stain (×135).

subependymal tissue. The ependyma normally consists of two layers: 1) of low epithelial cells lining the ventricular wall and 2) an underlying dense network of neuroglial fibers enclosing in their meshes numerous glial cells. Most attention has been directed toward the neoplasms deriving from the epithelial cells of the ependyma, reported in the literature as "ependymal gliomas" or "ependymomas." The latter have been studied exhaustively and have been fully established as a separate and well defined type of neoplasm. Their histologic character and derivation have been described in great detail by Bailey[1] and by Kernohan and Fletcher-Kernohan.[3] The latter have subdivided the ependymomas into four types: papillomas of the choroid plexus, epithelial, myxopapillary and cellular ependymomas. According to their degree of malignancy the tumors have been subdivided into two groups: ependymomas and ependymoblastomas. Attention was not directed to the

possibility of tumor derivation from the subependymal neuroglial elements.

More recently Globus and Kuhlenbeck[2] have stressed the significance of the subependymal cell plate (matrix) and pointed out its relationship to brain tumors of the ependymal type. They showed that the well developed subependymal cell plate is composed of three layers: 1) the ependymal cells lining the ventricular wall, 2) an underlying dense network of ependymal fibers, and 3) a layer of glial cells. The latter are considered as immature cell elements and as an important source for the development of certain

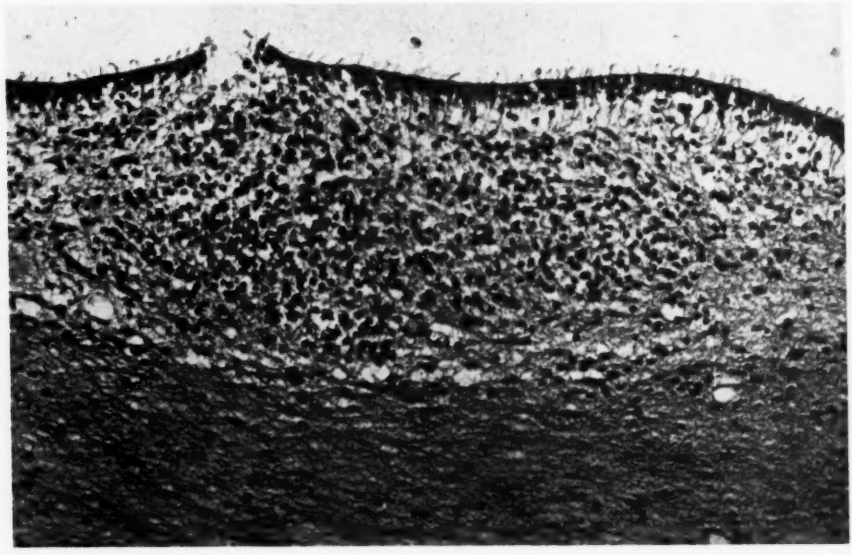

FIG. 7. Residuals of the subependymal matrix in the vicinity of the ventricular wall. Cresyl violet stain (×185).

types of tumors. In a series of nine neoplasms originating from the subependymal cell plate Globus and Kuhlenbeck were able to demonstrate that the tumor elements displayed a cell organization and cell morphology duplicating ependymal structures. One tumor was designated as cellular ependymoma, one as papillary ependymoma and two were classified as choroid papillomas. The remaining five tumors were identified as "spongioblastoma ependymale" and were described as a "primitive and malignant" tumor type. "It is characterized by the presence of undifferentiated spongioblasts, bipotential mother cells and occasional neuroblasts with many cells displaying mitotic activity." The authors came to the conclusion that even the more differentiated neoplasms of this series "must be considered as malignant."

There is strong evidence favoring the assumption that the series of tumors described in the present study were derived from the residual periventricular matrix layer, or the so-called subependymal cell plate. Conceivably certain portions of the residual matrix persist for a long period in postnatal life. Fig. 7 shows the presence of residuals of the subependymal plate as occasionally seen in the vicinity of the ventricular wall.

With these considerations in mind, it can be readily understood that whereas the tumors described as "ependymomas" duplicate the epithelial layer of the subependymal plate and thus assume the character of a well differentiated and highly specialized ependyma, the tumors described in this series derive from the subependymal neuroglial elements of the subependymal plate simulating neuroglial tissue and thus assume the character of mature glial tissue.

DIFFERENTIAL DIAGNOSIS

The location and the derivation of this group of tumors from the subependymal cell plate might lead to the conclusion that a close relationship exists between the "subependymoma" and the so-called "spongioblastoma ependymale" (Globus). In spite of their common point of derivation, there are significant differences between the two tumor groups. The spongioblastoma ependymale is according to Globus "characterized by the presence of undifferentiated spongioblasts, bipotential mother cells and occasional neuroblasts, with many cells displaying mitotic activity." The dominant cells forms in the tumors described in this study are such as to emphasize their far-advanced differentiation to fibrillary glia. Undifferentiated spongioblasts were not often encountered; neuroblasts were absent and mitotic figures were rarely seen. Whereas the spongioblastoma ependymale is according to Globus a "primitive and malignant tumor" there is plenty of evidence that the tumor reported in this study is a benign and well differentiated mature neoplasm. The spongioblastoma ependymale described by Globus corresponds to the ependymoblastoma of Kernohan and Fletcher-Kernohan and to the spongioblastic ependymoma described by Bailey and Cushing. The points of differentiation are therefore the same as those mentioned in relation to the spongioblastoma ependymale.

The differentiation from the cellular and papillary ependymomas as well as from the choroid papillomas can be easily made. These tumors usually assume the character of a well differentiated and highly specialized ependyma duplicating the epithelial layer of the lining ependyma, whereas the "subependymomas" duplicate mature glial tissue.

SUMMARY

A series of seven tumors has been described occurring in the vicinity of the ventricular system.

The dominant cell form and cell arrangement encountered in the tumors were morphologically indistinguishable from those present in the normal

subependymal glia. Because of this close relationship the term "subependymoma" has been suggested.

The "subependymomas" constitute a well defined group of gliomas with the following salient characteristics: a) The predominant cell is a mature fibrillary astrocyte. b) There is a great preponderance of glial fibers over cellular elements. c) The tumor is well demarcated from the surrounding tissue thus revealing an expansive type of growth rather than an infiltrating one. d) The expansion of the tumor is usually directed toward the ventricular space. e) Mitotic figures, giant cells and areas of necrosis are absent.

In view of the fact that all tumors displayed a cell organization and cell morphology duplicating the subependymal glia, it is concluded that they are derived from the residual periventricular matrix layer or the so-called subependymal cell plate.

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A METHOD FOR CONTROL OF CAROTID CEREBRAL CIRCULATION DURING OPERATION

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UNTIL quite recently intracranial aneurysms were mere autopsy room curiosities. Later, their presence was suspected before death but no active treatment was possible. Occasionally they were disclosed accidentally at operation, either to be viewed respectfully before the surgeon closed the wound or to be recognized only in an overwhelming hemorrhage. Now, in increasing numbers, they are being diagnosed and are being treated successfully in planned surgical attacks. Sudden, profuse hemorrhage continues to be the greatest obstacle to successful surgery in these cases. This complication usually is controllable, but often at the price of trauma to neighboring tissues by packing, electrocoagulation, or by silver clips applied through a pool of blood. At present, aneurysms on the intracranial portion of the internal carotid artery are, in this group, the most amenable to treatment since in the event of hemorrhage, the afferent vessel is easily controlled by the application of a single silver clip. A lesion on the anterior cerebral artery is much less easily dealt with, since profuse bleeding may occur by flow from the opposite anterior cerebral artery through the communicating vessel. Control of this may result in occlusion of both anterior cerebral arteries, which can be disastrous even though the systemic blood pressure is not allowed to fall below the normal level. Feeling that control of the carotid circulation might permit more precise occlusion of the affected vessels, the following technic was devised.

Draping is described in some detail so the entire operation may be done in one stage. The patient is postured for a frontal craniotomy, without turning the head. The scalp is prepared for operation and the line of incision is marked. The neck is prepared. A single wet towel is swung around the site of craniotomy to cover the brows and to leave the airway open (B, Fig. 1 a). The neck is then draped (Fig. 1 b) and two towels (C) are brought along the sides of the face and fastened above the craniotomy site. A towel (G) is placed temporarily across the lower face. The common carotid arteries now are exposed through small oblique incisions in the line of skin folds at the level of the lower border of the thyroid cartilage. A stout, 36-inch linen ligature then is passed around the artery (Fig. 2 a). A "whistle-tipped," woven, semi-flexible catheter (#18 F.) is threaded with a wire on the end of which a hook is formed. Both strands of the ligature then are drawn through the catheter with the hook, which is discarded. The tip of the catheter is placed on the artery and by traction on the ends of the ligature, one may occlude or release the artery at will (Fig. 2 b). The wounds are closed around the catheters with a few buried sutures and skin clips (Fig. 2 c). The towel (G) is removed and a fresh towel (D, Fig. 1 c) is put across the upper face. The catheters are brought around the face to the craniotomy site. The center of another towel (E) is placed under the chin and the ends are brought upward, protecting the part of the catheters outside the head drapes to give the anesthetist freedom of action. The head then is turned as desired and the craniotomy site is

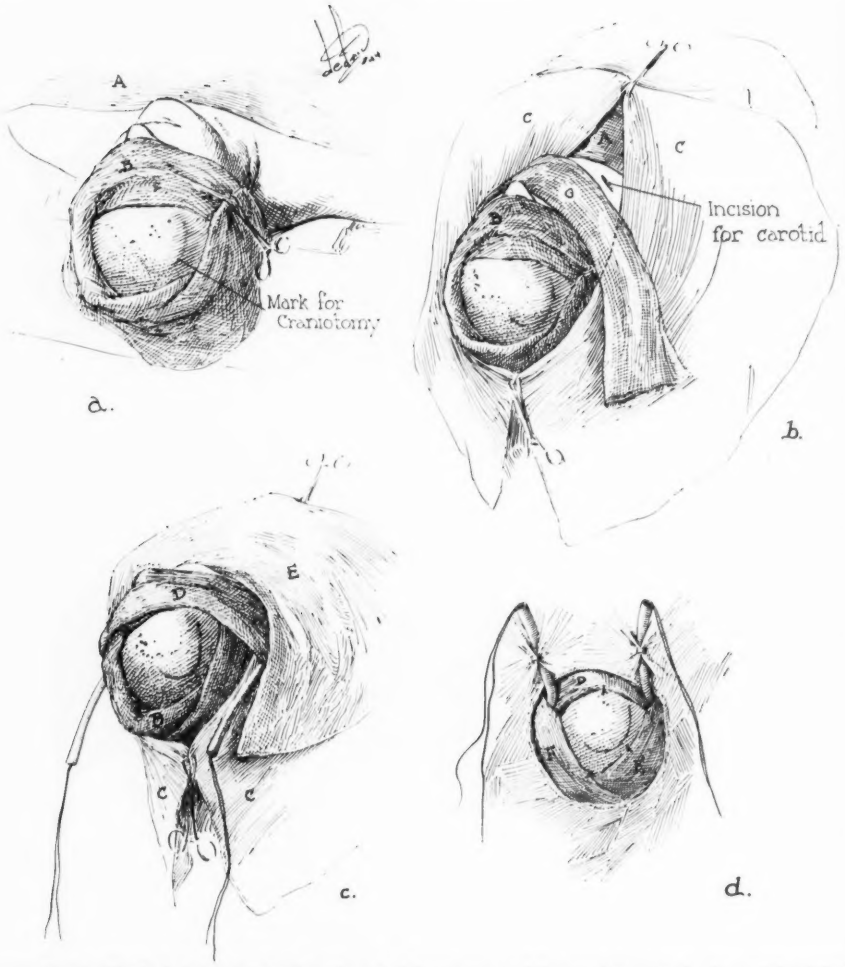

FIG. 1. Method of draping to allow the arterial exposure and the craniotomy to be done with minimal redraping. The towels are lettered in order of their application. (a) Scalp and neck prepared; craniotomy and carotid incisions marked. A mark is placed similarly over the left carotid artery. (b) Towel G covers the lower face and towels C protect the field from below. (c) After the carotid operations, towel D is applied as a part of the permanent draping for craniotomy. Towel G is replaced by E to protect the neck and to give the anesthetist unrestricted access to the nose and mouth. (d) The completed craniotomy draping, with the catheters in the field.

draped in the usual manner (Fig. 1 d). The ends of the catheters with their ligatures are left exposed, fastened to the head sheet with skin clips.

The craniotomy then is performed and the lesion is exposed. If hemorrhage occurs, an assistant holds each catheter with one hand and with the other makes firm, gentle traction on the ligatures. This obliterates the carotid flow so that within a second or two the field may be cleared by suction. The bleeding spot may be found and a silver clip placed to control a vessel

on one side of it. The assistant then releases the carotid compression on that side and the other side is dealt with. To prevent misjudgement of time, a nurse watches a clock with a sweep second hand and calls off the seconds. Whether necessary or not, we have not maintained uninterrupted occlusion for more than ten seconds. If longer time is required to control

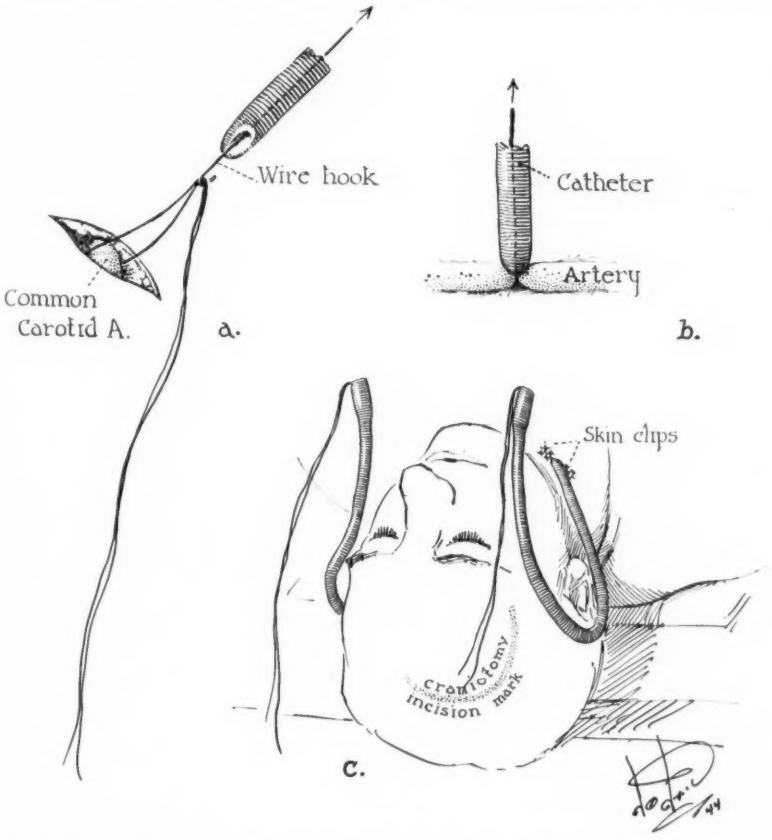

FIG. 2. Detail of ligature and catheter placement. (a) Linen ligature around artery being drawn through catheter with wire hook. (b) Occlusion of artery by tightening ligature against tip of catheter. (c) Skin incisions closed with clips. Catheters brought into craniotomy field.

bleeding, the point is covered with a carefully placed cottonoid or muscle pack. After allowing circulation to proceed for a few minutes, the vessel again may be occluded and permanent control of the bleeding point be obtained.

After the craniotomy wound is closed, the drapes are removed. The catheter is withdrawn slowly from the neck incision. One strand of the ligature is cut at skin level and the other end is withdrawn from around the artery. Another skin clip is applied if the catheter tract gapes. The neck wounds are dressed separately with small gauze squares and adhesive tape.

We have used this method in only two cases. In one the lesion proved not to be an aneurysm but in the other it facilitated the operation considerably.

The preliminary arterial surgery requires about 35 to 45 minutes, but in the case of a difficult aneurysm the procedure probably will save a great deal of time and trauma. The procedure is being reported now, rather than after being used in a larger number of cases, so other neurosurgeons may have an earlier opportunity to use and evaluate it.

CONCLUSION

A method is offered to provide positive control of the carotid cerebral circulation, to facilitate attack upon intracranial arterial aneurysms.

ARNOLD-CHIARI DEFORMITY IN AN ADULT WITHOUT OBVIOUS CAUSE

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THE TERM "Arnold-Chiari Deformity" is generally used to designate a specific modification in the configuration and location of the hindbrain.[3,4] With this deformity this portion of the nervous system is narrowed laterally and elongated in its axial diameter so that the lowermost portions of the medulla oblongata and the cerebellum extend through the foramen magnum into the vertebral canal. This deformity is frequently associated with a relative stenosis of the aqueduct of Sylvius and with abnormal stretching of the lowermost cranial and the upper cervical spinal nerve roots (Lichtenstein[7]).

It is found very frequently in infants suffering from extreme degrees of spina bifida (Arnold,[3] Chiari,[4] Lichtenstein,[7] Schwalbe and Gredig,[10] and Jacob[6]). Its occurrence in adults has generally been in conjunction with bony anomalies of the craniovertebral junction, such as basilar impression, or platybasia, and fusion abnormalities of the cervical spine (Klippel-Feil's syndrome). Examples of such combinations have been reported by List[8] and by Gustafson and Oldberg.[5] The occurrence of an Arnold-Chiari deformity of sufficient magnitude to produce very marked neurological symptoms with no evidence of a spina bifida or of any bony anomaly in the cervical region is most unusual.

REPORT OF CASE

Case #151-279. The patient A.B.J., an American negress with part Indian blood, aged 40 years, was admitted to the outpatient division of the Department of Neurology and Neurological Surgery on Oct. 26, 1942. She stated that she had been perfectly well until August 1942, when, after a day of unusually hard work, her legs gave way and she slumped to the floor. In a few minutes she arose and seemed perfectly well. The following morning she experienced weakness in both lower extremities and was forced to use a cane for support. Two days afterwards she experienced weakness in the entire right upper extremity and had particular difficulty in moving her fingers. This was followed by tingling paresthesias in the right upper and both lower extremities as well as by sharp knife-like pains which were most severe in the calf of the right leg and in the region of the right elbow. The paresthesias persisted and the pain occurred intermittently. She developed a subjective feeling of numbness in the affected parts.

In her past history nothing of significance was noted. She had suffered from otitis media on the right side since childhood and had had a single attack of acute arthritis of the left ankle in August 1932. In 1923 some pelvic operation had been performed at the Cook County Hospital. She had given birth to six children and had had one spontaneous miscarriage. Her family history revealed nothing of significance.

Neurological examination on Oct. 26, 1942 showed deviation of the tongue to the right, decreased motor power in the right upper and in both lower extremities, stereoanesthesia

in the right hand, patchy hypesthesia and hypalgesia in the right upper extremity, and loss of vibration sense at the ankles. On Oct. 30, 1942 it was noted that she walked slowly and laboriously and that Hoffmann's sign could be elicited on the right side. On Jan. 25, 1943 atrophy and fibrillary twitchings of the right side of the tongue were noted for the first time. The deviation of the tongue to the right was marked and hypalgesia was found on the right side of the body with the exception of the face. At this time a vascular lesion at the level of the hypoglossal nucleus was considered as a probable diagnosis. A subsequent examination on Mar. 1, 1943 revealed, in addition to the aforementioned findings, bilateral foot drop with absent Achilles' reflexes. On July 19, 1943 nystagmus was noted and on Oct. 4, 1943 her gait was very feeble and marked pitting edema of both feet and ankles had developed. Because of the atypical clinical picture the patient was admitted to the Illinois Neuropsychiatric Institute, the Neurological and Neurosurgical Division, on Nov. 15, 1943 for further studies.

A summary of the positive findings in the detailed neurological examination performed on Nov. 15, 1943 follows.

Cranial nerves. III, IV, and VI: Sustained rotary counterclockwise nystagmus in all directions of gaze but most marked on looking to the right. XI: Weakness of elevation of the right shoulder. XII: Deviation of the tongue to the right with marked atrophy of the right side and very obvious fibrillary twitchings. Fine fibrillary twitchings in the left half of the tongue.

Motor. Marked weakness of the right upper and lower extremities.

Sensation. Hypesthesia and hypalgesia of the right side of the body, excluding the face, of patchy distribution but most marked in the leg, hand and shoulder. Hypesthesia and hypalgesia of the left foot. Loss of vibration sense in both ankles. Stereoanesthesia in the right hand. The coordination test of placing the finger to the nose revealed marked ataxia with decomposition of movement on the right side.

Reflexes.	*Superficial*	Abdominals absent		
	Deep	Patellar	Rt. +++	Left +
		Achilles	Rt. 0	Left 0
		Biceps	Rt. ++	Left +
	Pathological	Hoffmann	Rt. +++	Left +
		Babinski	Rt. 0	Left 0

Spinal puncture performed on Nov. 17, 1943 revealed a complete subarachnoidal block, the initial fluid pressure being 40 mm. of fluid. The cerebrospinal fluid was clear, colorless, and contained only one cell per c. mm. The Pandy and Wassermann reactions were negative and the total protein was 40 mg. per cent.

Because of the spinal block, diagnoses of syringobulbia and of intramedullary tumor at the level of the foramen magnum were proposed as well as the diagnosis of a neurinoma arising from the right hypoglossal nerve.

Roentgenograms of the skull, the foramen magnum and the cervical spine failed to reveal significant alterations.

A suboccipital exploration was performed on Nov. 26, 1943 under local anesthesia. Upon removal of the central portion of the occipital bone overlying the cerebellum and including the posterior part of the foramen magnum, the dura mater was found to be taut and bulging. The posterior arch of the first cervical vertebra was then removed. Upon incision of the dura mater a typical Arnold-Chiari deformity was encountered. The medulla oblongata and the tonsils of the cerebellum were displaced into the upper portion of the cervical spinal canal (Fig. 1). The right hypoglossal and spinal accessory nerves were found to be elongated and tense. The fourth ventricle and the space beneath the cerebellum on either side of the bulb was carefully explored. No tumor was found. The lower part of the fourth ventricle lay below the level of the foramen magnum. Blunt cannulae were inserted into the substance of the cerebellum without encountering any unusual resistance or any cystic cavity. Except for the downward displacement the cerebellum and the brain stem appeared normal.

The dura mater was left open over the cerebellum and upper spinal canal, and the wound was closed. In the course of the ensuing three weeks the patient gained considerable strength and the sensory alterations improved. From Nov. 22, 1943 to Dec. 18, 1943 she received physiotherapy in the form of massage, faradic stimulation and passive motion. Before discharge from the hospital on Dec. 19, 1943 the Achilles' reflexes were found to have returned.

Reexamination on Jan. 13, 1944 revealed that she walked without aid. The Achilles' reflexes were more active, being greater on the right side. On January 21 the improvement was found to be even more marked and the atrophy of the right half of the tongue, though still unmistakable, was much less marked than formerly.

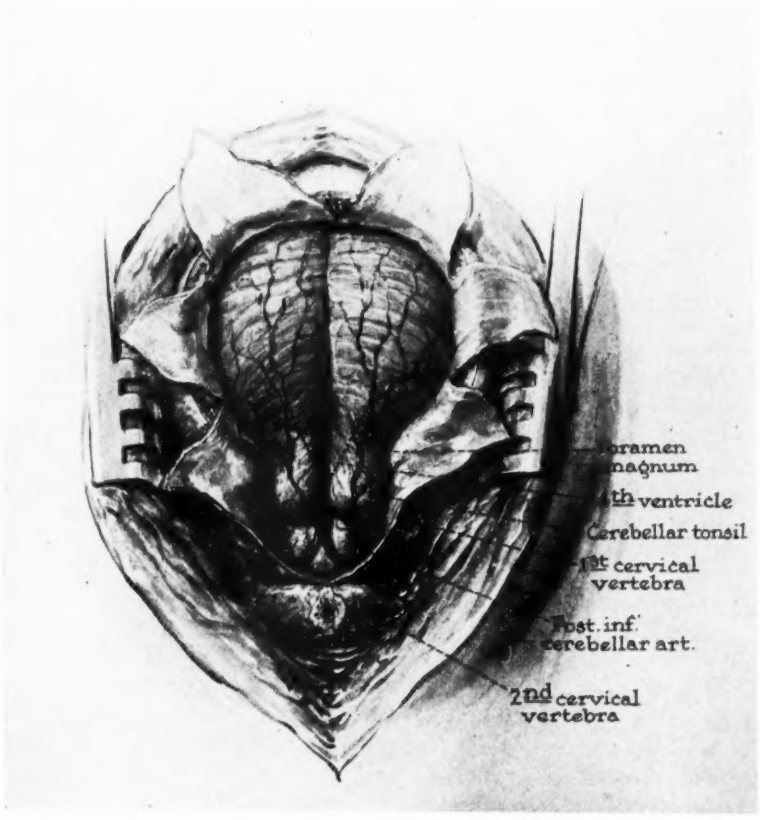

FIG. 1. Drawing of the operative exposure, elaborated from the operator's sketch. The cerebellar tonsils have herniated through the foramen magnum to the level of the atlas. The postero-inferior cerebellar arteries curve downward almost to the level of the 2nd cervical vertebra.

DISCUSSION

Clinical Considerations. The weakness and sensory disturbances in the

extremities coupled with the atrophic paralysis of the right side of the tongue and the complete subarachnoid block on lumbar puncture were indicative of an expansile lesion at the level of the foramen magnum. The absence of bony anomalies and the age of the patient misled the observers, for the possibility of an Arnold-Chiari deformity was not even considered. Adams, Schatzki and Scoville[1] have divided the signs and symptoms occurring in the symptomatic varieties of the Arnold-Chiari deformity into four groups:

1. Those resulting from increased intracranial pressure, such as choked discs and headache.

2. Those indicative of involvement of the lower cranial nerves.

3. Pyramidal signs and sensory disturbances resulting from compression of the brain stem or spinal cord.

4. Cerebellar signs, such as gait disturbances and poor coordination. This symptomatology, coupled with the demonstration of a characteristic roentgenogram of the subarachnoid block in the cervical region after the intraspinal injection of an opaque oil, is very suggestive of the Arnold-Chiari deformity.

In our case there was no evidence of any increase in the intracranial pressure. The ataxia on the right side may have resulted from pressure on the spinocerebellar pathways. As in most other cases reported in the literature, the symptomatology of the disorder became fully developed one or more years after the onset. Many times the earliest signs are ignored, as were the pains in the base of the skull which were present for two years in Case I of Adams *et al.*[1] This 17 year old boy's main symptoms were dysphagia and difficulty in walking due to stiffness and unsteadiness of the lower extremities. Lumbar puncture revealed a complete subarachnoid spinal block, and the x-rays of the cervical spine following the introduction of lipiodol were diagnostic.

In the case described by Aring,[2] that of a 20 year old boy, the onset had occurred 18 months before hospitalization with unsteadiness of the lower extremities and dysphagia. Neurological examination revealed weakness of the right side of the palate and fascicular tremors throughout the tongue in addition to the ataxic gait, slurred speech and nystagmus. As in the aforementioned case no evidence of spina bifida was seen.

Anatomical Considerations. The pathogenesis of the Arnold-Chiari deformity has not been decided with certainty in all instances and many views have been presented. In the earlier descriptions it was considered a malformation, but the general consensus today is that it is more likely a deformity resulting from a change in the relationship of the hindbrain to its bony envelope.

One pathogenic factor responsible for such a deformity has seemingly been established with certainty. This is the abnormal fixation of the spinal cord and/or its meninges and roots by a spina bifidous defect. Such fixation prevents the normal ascent of the spinal cord with the growth of the vertebral column and development of the cauda equina. The greater the defect

and the more caudal its location, the earlier is the appearance of the deformity and its train of complications. In many instances described by Lichtenstein[7] the defect was already present at birth. Since the cerebellum is not fully developed at that period, abnormalities in its architecture occur which presumably result from its growth in an abnormal environment. The Arnold-Chiari deformity, thus, often presents evidence of maldevelopment particularly in the cerebellum, which may be small and contain dysplastic folia. In the case reported by Penfield and Coburn,[9] in which the spina bifida defect occurred in the thoracic region and was successfully operated on in childhood, the complicating symptoms of the Arnold-Chiari deformity did not appear until the patient was 29 years of age.

A second factor responsible for the Arnold-Chiari deformity appears to be platybasia which, like spina bifida, is basically an anomaly in the development of the perinotochordal mesenchyma. In platybasia the base of the skull is flattened and the foramen magnum is elevated into the posterior cranial fossa. Seemingly because of the diminution in size of the infratentorial space and the upward dislocation of the foramen magnum, the lowermost portions of the hindbrain are forced through the foramen magnum. This does not occur in all instances, for frequently there is only impingement on the neuraxis without any great change in the neural-bony relationship.

Of unusual interest, however, are cases like the one we are reporting, in which no evidence of platybasia or spina bifida is encountered. In an effort to find the etiology of the deformity in our case, lipiodol was injected into the lumbar subarachnoid space in an effort to outline the caudal sac and the sacral nerve roots. No unusual findings were observed. It appears that even under perfectly normal conditions of development the hindbrain is subjected to a force that tries to draw it into the vertebral canal. We know that the rate of growth of the vertebral column is greater than that of the spinal cord. As a result the caudal portion of the spinal cord ascends (forming the cauda equina). This transformation must be associated with some downward pull upon the cervical spinal cord and the brain stem. This force is generally neutralized, however, by the firm fixation of the brain in the cranial cavity. The present case would make it seem likely that on occasion these forces can produce an Arnold-Chiari deformity in the absence of any unusual anchorage of the spinal cord or of any bony anomaly. It is possible that minor degrees of this deformity that are asymptomatic may occur, but careful anatomical studies, which are lacking, would be necessary to prove their presence.

SUMMARY

An Arnold-Chiari deformity in a 40 year old negress without evidence of a bony anomaly is reported.

The paralysis, sensory disturbances and complete subarachnoid block resulted from pressure of this deformity on the unyielding bony rim of the

foramen magnum. Surgical decompression of the craniovertebral junction resulted in very marked improvement in the clinical picture.

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THE PHANTOM LIMB SYNDROME
A DISCUSSION OF THE ROLE OF MAJOR PERIPHERAL NERVE NEUROMAS

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FOLLOWING major extremity amputation a large proportion of patients will retain quite specific impressions of their missing limb, persisting for months, years, or as long as they live. Weir Mitchell[8] studied a series of 90 major amputations during and after the American Civil War, and in 86 of these cases found characteristic "phantom" limb symptoms. More recently Leriche,[4] Livingston,[5,6,7] Bailey and Moersch[1] and others[9,10,12] have emphasized the frequency and uniformity of this phenomenon following amputation.

Such phantom limb symptoms become clinically important when associated with protracted or severe pain, However, of all patients with well-defined phantom limb sensation, comparatively few (probably less than 10 per cent) will have severe persisting pain referred to the phantom limb. In a majority of these cases the first attempt to obtain relief has been through resection of major nerve neuromas. Neuromas subjected to mechanical insult from muscle traction, lack of soft-tissue protection, pressure of prosthesis, etc., may become a source of real pain. In such cases removal of the neuroma and protection of the area from mechanical trauma will relieve the symptoms. This pain is always directly dependent upon the traumatic factors and is readily differentiated from true phantom limb pain. In true phantom limb pain clinical results of neuroma resection have been generally disappointing,[1,6,8,9,10,12] and the role of the major peripheral nerve neuromas, both in relation to the phantom limb impression itself and in phantom limb pain, has remained confused.

The principal studies of the phantom limb phenomenon have been concerned with patients having serious pain. Attempts to determine the role that the neuroma plays in such cases is frequently difficult since any disturbance of the stump is likely to aggravate pain in the phantom limb. This aggravation may occur when the neuroma is disturbed, but it may also be set off by bumping the stump, pinching the skin, tapping the bone end, rubbing the scar, etc. However, in patients having definite and characteristic phantom limb symptoms *without* severe pain, the neuroma may be more readily studied, and its relation to the phantom limb impression and to phantom limb pain may be more accurately examined. This study is based on such cases.

Forty-two patients with a total of 50 major extremity amputations were

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studied in detail.* The group is representative of amputation in civilian life. The primary causes for amputation were: vascular disease, 36 per cent; trauma, 28 per cent; infection, 16 per cent; tumor, 8 per cent; miscellaneous, 12 per cent. Age at the time of study ranged from 19 to 79 years. It is interesting to note that the two patients who had the earliest amputations, done at 9 and 12 years of age, had clearly defined phantom limbs 33 and 38 years after amputation although neither patient had had severe pain disability during that period. The longest duration of phantom symptoms in the group was 44 years.

The principal characteristics of the phantom history were carefully studied in these cases and found to conform accurately to the findings in other series. Of the 50 amputations only one was never associated with phantom limb symptoms. Seven patients with eight amputations were followed from the time of surgery particularly to record the time of onset and original pattern of the phantom symptoms.

There are certain features of the phantom limb syndrome that are important in considering the part the neuroma may play in this phenomenon. First, is the geography or pattern of the phantom limb, particularly in relation to the sensory patterns of the major peripheral nerves; second, is the time of onset of phantom limb symptoms following amputation; and third, is the relation of phantom symptoms to the mechanical and irritative disturbances in the stump that might be expected to alter the state of the neuroma.

The phantom limb is not a simple total reproduction of the amputated extremity. There is a definite patterning of the phantom limb which does not conform to the geography of the major peripheral nerves. In the upper extremity amputations the fingers are most prominent, although in many instances only the palmar surfaces of the finger tips are actually represented. The palm is less frequently felt, and the wrist and dorsum of the hand are usually not present. The forearm and upper arm are rarely perceived. Many patients give the impression that they feel "the whole thing," but on careful questioning it is evident that the posture and presence of much of the phantom limb is inferred, often from small portions of the hand or fingers of which the patient has very specific impressions. In lower extremity amputations similar phantom patterning is found. In neither extremity does the pattern correspond to the major peripheral nerve distributions. It was not possible, for instance, to describe any of the phantom limbs as representing an ulnar neuroma or irritation, or peroneal neuroma or irritation, with resulting "ulnar" or "peroneal" phantoms. In addition there was no tendency for the phantom pattern to "spread" from a primary nerve pattern to a more complex pattern during its initial stages, in patients studied immediately following amputation. The geography of the phantom limb was not affected in any of these cases by serious local complications, such as stump sepsis or

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osteomyelitis, and frequently had failed to change following stump revision, neuroma resection, or re-amputation. Since such disturbances must alter the status of the neuroma, the lack of change in phantom pattern during such periods is significant.

The time of onset of phantom symptoms is of considerable interest. A majority of these patients felt that their phantom limbs had been clearly established immediately or very soon after amputation. Of the seven patients studied from the time of amputation, all were able to describe their phantom limbs accurately within a period of a few hours to a few days following amputation. This experience is not unusual, as Weir Mitchell (p. 349)[8] has emphasized: "The sensation of the presence of the part removed exists in many persons as soon as they come from under the influence of the anesthetic used at the time of the amputation." The pattern of the phantom does not change significantly during the healing period. There are changes in the intensity of symptoms in many cases, and frequently changes in the posture, size, tension, and mobility, but the geographical area represented in the phantom limb shows a remarkable constancy. Many patients stated that in this respect their phantom limb was unchanged, often over a period of many years, from the time they first became conscious of the phantom sensations.

The neuroma is not established early enough to be the determining factor in these initial symptoms. The traumatic "neuritis" following nerve section and preceding neuroma formation is not a static process and might be expected to produce a less stable pattern. Furthermore, if the neuroma were the inciting factor in these symptoms, the various forms of surgical treatment of the nerve end at the time of operation might be expected to produce differences in the time of onset and in the character of the phantom symptoms. Several types of treatment of the major nerves were utilized in this series, singly or in combination—simple high division, crushing, alcohol injection, and proximal ligation. There was no evidence that any discernible variation, either in time of onset or in pattern of symptoms, resulted from these various methods.

In the literature many methods of treatment of the central end of the divided nerve in an effort to prevent neuroma formation have been reported. These include crushing, ligating, freezing, or cauterizing the nerve end; various types of plastic closure of the nerve sheath, and the injection of phenol, formalin, or absolute alcohol above the nerve end. Clinically, the injection of absolute alcohol above the nerve end has been widely employed. Experimental studies of Huber and Lewis,[3] showed delay in fiber regeneration beyond the nerve end, but clinical studies have not shown a significant decrease in the frequency or size of neuromas, or a reduction of the incidence of phantom limb symptoms or of phantom limb pain with this method. More recently Guttmann and Medawar[2] have experimentally demonstrated quite prolonged inhibition of regeneration at the nerve end by the injection of 40 per cent formalin into a relatively long proximal segment of the divided

nerve. Variations in the amount of intraneural disorganization and necrosis produced by these different methods, and particularly the length of nerve destroyed above the level of section, will determine the delay in regeneration of fibers beyond the nerve end. However, the cell body and nucleus which govern the growth tendency of the motor and sensory axons lie in the anterior horn and posterior root ganglion, so that damage to a small and distal segment of the axon can be expected to delay but not prevent the attempt at regeneration that results in neuroma formation. Each of these technics of treating the nerve end has had clinical trial, but there has been no substantial evidence that the incidence of the phantom limb impression or of phantom limb pain has been significantly modified by such treatment.

In 14 of these patients with 20 amputated limbs, a total of 30 major nerve neuromas were accessible and could be accurately identified. In all but one of the amputations the corresponding phantom limb was clearly defined. On vigorous palpation of the neuroma, most of the patients described their sensation as like "striking your funny-bone." In 14 of the neuromas such stimulation produced only local pain or pain referred proximally in the stump. In the remaining 16 stimulation produced pain which was also referred distally and in each case the distribution of pain corresponded to the normal pattern of the stimulated nerve. *In no case did stimulation of the neuroma excite or simulate typical phantom sensations.* In two patients with forearm amputations in whom the three major nerves could all be identified, the neuromas were stimulated with faradic current. This electrical excitation again produced sensation which conformed to the peripheral nerve distribution and to a less striking degree produced appropriate motor activity in the phantom hand. Weir Mitchell (p. 359)[8] reported similar experience with electrical stimulation of neuromas.

COMMENT

There is no evidence from this study that the major peripheral nerve neuroma is responsible for the phantom limb impression. The high incidence of phantom limb impression following amputation, its early appearance, and its stability in the presence of varying states of the stump tissues and nerves, suggest a central rather than a peripheral denominator for these symptoms.

The occurrence and persistence of severe phantom limb pain in a comparatively small proportion of the patients with phantom limb symptoms, suggest an irritative disturbance that is superimposed on the underlying phantom limb mechanism. Evidence from these observations and from clinical experience suggests that the major peripheral nerve neuroma is very rarely the "key" factor in this irritative process.

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AN IMPROVED CLINICAL DERMOHMMETER*

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INTRODUCTION

IT HAS BEEN shown by Richter and his associates[1] that measurements of the electrical resistance of the skin provide an accurate and objective means of diagnosis in peripheral nerve injuries. Areas of high resistance may be mapped out with a small exploratory electrode held in the hand, with the reference electrode attached to the ear lobe that has been punctured with a pin prick to eliminate its skin resistance. These areas of high resistance represent skin that has lost its sympathetic nerve supply. They can be outlined with a high degree of accuracy and usually correspond closely to the area accurately mapped as analgesic or anaesthetic, and may be related only to an area of hypaesthesia. The high skin resistance is due principally to the inactivity of the sweat glands in a denervated area.

The "dermometer" recommended by Richter, and accepted as standard issue by the U. S. Army Medical Corps, was found to possess certain disadvantages which stimulated the design of a different model to recommend for Canadian service. Such an instrument should be much more "fool proof" in operation (e.g., in the Richter instrument the meter will be severely damaged if the testing electrodes are accidentally placed in contact with each other).

SPECIFICATIONS

The dermohmmeter is mounted in a wooden box measuring $8\frac{1}{2} \times 8 \times 8$ inches, as shown in Fig. 1. Its total weight, including electrodes and electrode paste contained in a special compartment in the cover, is 7 pounds. It consists principally of nine standard flash-light batteries, a 0–50 microammeter, with a special contact on its deflecting needle which prevents overload, a double pole 7 contact Yaxley switch, seven fixed resistors, and two binding posts.

The wiring diagram is shown in Fig. 2. Six separate sensitivities are provided by the six contacts on the tap switch S_1, which connects different numbers of batteries giving 1.5, 3.0, 4.5, 7.5, 10.5 and 13.5 volts. This method of sensitivity control eliminates the necessity of constant current drain from a potentiometer across the batteries. Also no current can flow from the batteries unless a contact is made between electrode terminals (E).

As the voltage is increased, the resistance in series with the meter is increased in such a manner that the current flowing would equal 500 microamperes should there be a short circuit between the binding posts at E. This would burn out the 0–50 microammeter were it not for the platinum leaf contact in the meter, which is closed at full deflection of the needle. This immediately reduces to one tenth the current passing through the meter.

The measurement of resistance values to an accuracy of 4 to 5 per cent

* This paper is a report on an investigation carried out for the Associate Committee on Army Medical Research, National Research Council, Ottawa, and the Research Division, Director General of Medical Services, National Defence Headquarters, Ottawa, Ontario, Canada.

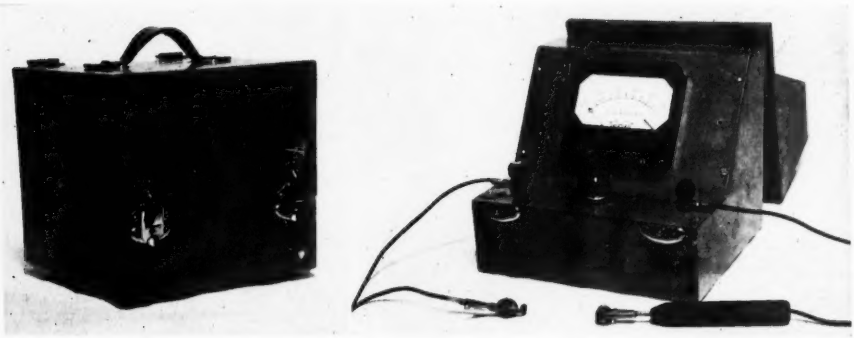

FIG. 1. Clinical dermohmmeter, shown (left) closed and (right) ready for use. Dimensions: 8½×8×8 inches. Weight: 7 pounds. All accessories are contained in the cover, which is turned back during use.

may be obtained from calibration curves provided (Fig. 3). This is sufficiently accurate for clinical purposes. In mapping a high resistance area it is more important to have a sharp delineation than to have accurate measure-

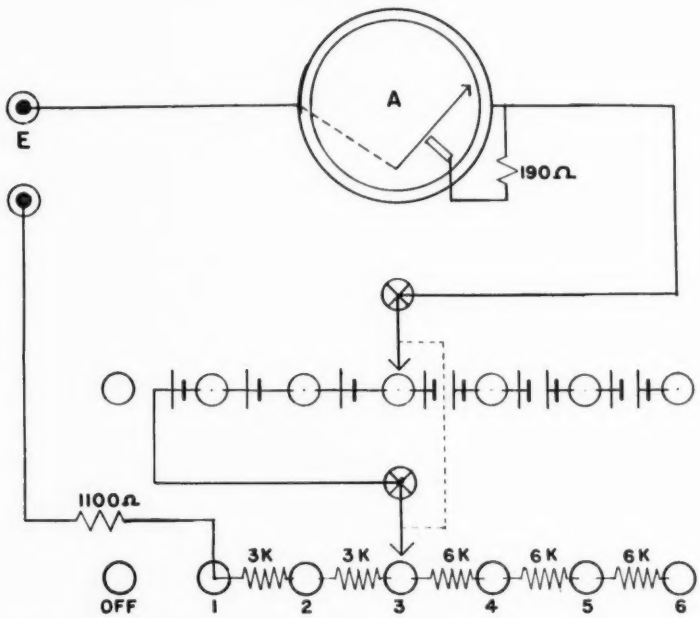

FIG. 2. Wiring diagram of dermohmmeter. The meter used (A) is a 0–50 microammeter with a special platinum contact to the deflecting needle. The testing electrodes are attached to the binding posts (E). Six sensitivities are provided by turning the ganged rotary switches (S_1) and (S_2). See text for further description.

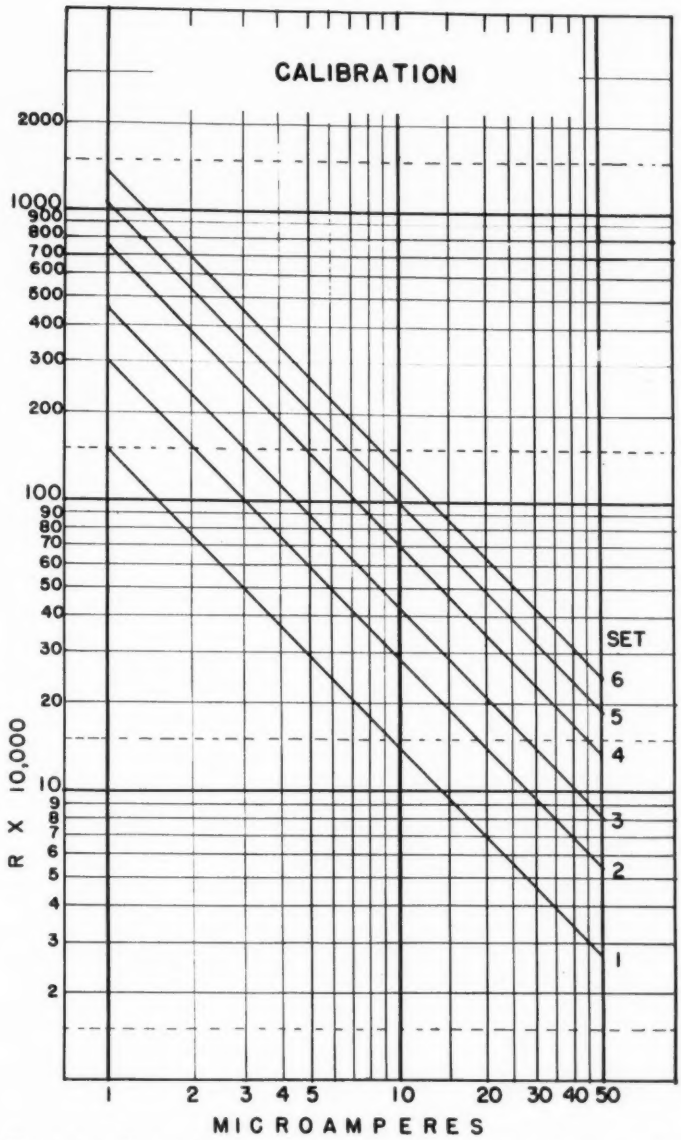

FIG. 3. A double log plot of dermohmmeter calibration for each of six sensitivities.

ment of absolute resistance values, although the latter may be important in judging recovery in the course of re-examination. Sharp delineation is provided by the potential overloading the meter by a factor of ten.

The range of resistance covered by this dermohmmeter is from 27,000 ohms to 13,500,000 ohms, which has been found to be adequate for all clinical cases encountered to date, and extends by about 3 times the range of the Richter instrument. This extension of range minimizes the necessity for causing the individual to perspire before clear differentiation can be made between denervated and adjacent normal skin.

CONCLUSIONS

A clinical dermohmmeter is described for use in the diagnosis of peripheral nerve injuries. It has the following principal characteristics:

1. The instrument is small and self-contained with all accessories. (Dimensions: $8\frac{1}{2} \times 8 \times 8$ inches. Weight: 7 pounds.)

2. A wide range of resistance values, 27,000 ohms to 13.5 megohms, may be measured with an accuracy of 4 to 5 per cent.

3. Sharp delineation of denervated skin areas is obtained by potentially overloading the meter by a factor of 10, at each of six sensitivities.

4. The meter is completely protected against damage from short circuit of the testing electrodes.

5. Long life of standard flash-light batteries is assured by circuit design which eliminates a potentiometer across the batteries and by making it impossible to close the box without the current being effectively turned off.

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STUDIES OF ELECTRICAL SKIN RESISTANCE IN PERIPHERAL NERVE LESIONS*

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INTRODUCTION

CHANGES in electrical skin resistance have been reported by Richter and his associates,[5,8,10] on the basis of extensive experimental and clinical studies to provide an accurate and practical clinical test for peripheral nerve injuries. They have designed a simple apparatus for this purpose which is now on issue to the U. S. Army Medical Corps.

Areas of skin deprived of their sympathetic nerve supply show a marked increase in electrical skin resistance as compared to surrounding normal areas containing active sweat glands. This is due largely to the inactivity of sweat glands in the denervated skin. Differences in surface moisture can be usually seen or felt, and the areas of high resistance coincide with the absence of sweating, as shown by the Minor starch-iodine test. Vasodilatation plays a very small role, if any, in these skin resistance changes. Vasodilatation produced by (1) prolonged application of a blood-pressure cuff caused no consistent changes in skin resistance, and (2) vasodilatation by niacin failed to produce a significant change (confirmed by one of us in initial experiments).

The difference in resistance becomes greater and the line of demarcation between denervated skin and surrounding normal areas becomes sharper as the normally innervated sweat glands are stimulated, either by increasing the surrounding temperature, increasing body metabolism, or by certain drugs that stimulate the sweat glands through the sympathetic nervous system. Under optimal conditions, the transition from an area of high resistance to an area of low resistance is very sharp, usually detected by movement of the testing electrode about $\frac{1}{8}$ of an inch. Areas of high resistance usually correspond exactly to accurately determined areas of sensory loss.

Experimental studies of skin resistance changes in animals following sympathectomy (Richter[2,4]) have shown that there is an initial rise, which shortly reaches a very high level and falls, in the monkey, after several months, to a permanent level still far above that observed preoperatively.

METHODS

The methods used were essentially the same as those outlined by Richter and his associates.[16] A small D.C. current (maximum of 50 microamperes) was passed through the skin and the change in resistance from a denervated

* This paper is a report on an investigation carried out for the Associated Committee on Army Medical Research, National Research Council, Ottawa, and the Research Division, Director General of Medical Services, National Defence Headquarters, Ottawa, Ontario, Canada.

to a normal skin area indicated on a sensitive meter. Representative values of resistance in ohms were recorded. In experimental studies with animals, the resistance of the central foot pad of the hind limb was measured on both sides after section of one sciatic nerve.

Various ohmmeters have been used, including several commercial instruments and special designs. Recently a new dermohmmeter has been designed by one of us which has proven most satisfactory. The details of this instrument have been described in a separate communication.* In initial experiments with animals an especially designed A.C. and D.C. instrument

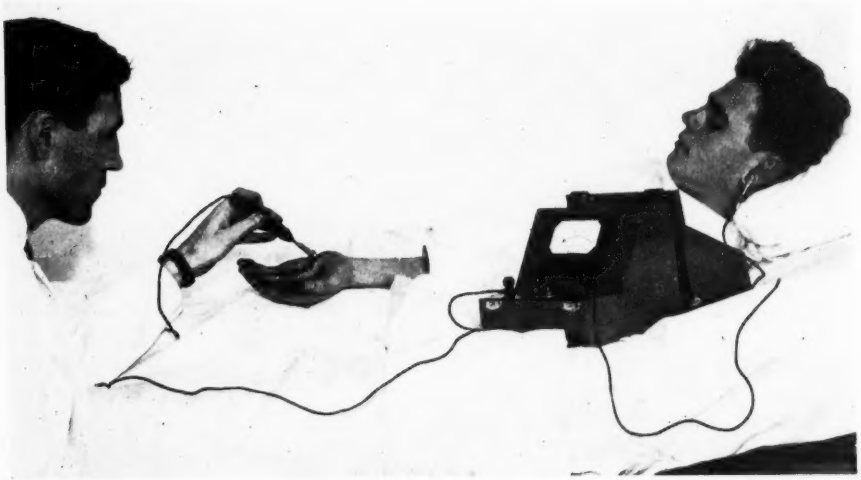

FIG. 1. Photograph of dermohmmeter with ear clip attached to patient, and handle with the roller electrode inserted.

was employed in order to assess the merits of these two types of measurement. Extremely high values of resistance encountered in animal studies were measured with the R.C.A. "volt-ohmyst."

The fixed electrode consisted of a silver clip which was attached to the ear. The resistance of the lobule of the ear was first greatly reduced by rubbing the lobule with electrolytic jelly. The jelly, when rubbed in, made the resistance at this point so low that it was not found necessary to puncture the skin with a pin as has been recommended (Richter and Woodruff[9]), even though this does reduce the resistance at this point still further.

The exploratory electrode consisted of a bakelite handle with a socket into which could be fitted various forms of electrode. These electrodes consisted of flat silver discs (4 and 9 mm. in diameter) mounted on a copper rod

* See page 257 of this issue of the *Journal*.

and a roller electrode, as illustrated in Fig. 1. This latter type has proven very satisfactory, particularly for the rapid mapping of larger areas. It can be rolled over the skin from a high to a low resistance area, keeping contact with the skin at all times.

We found, initially, considerable difficulty in obtaining accurate results in some patients due to inadequate sweating of normal skin areas and to cumbersome methods of diaphoresis. This was particularly true with spinal cord injuries and sympathectomies. In most cases of peripheral nerve injury satisfactory results could be obtained, especially with the new dermohmmeter, without artificial diaphoresis. The use of overheated rooms, bakers, electric blankets, hot drinks, and aspirin in our initial studies were so unsatisfactory that the routine use of this test was discouraged.

Following the work of Guttman[1] on the use of furmethide in testing sweat secretion in man, we have used this drug (2.5 to 5 mg. subcutaneously) in certain cases to clarify skin resistance measurements. This is a parasympathomimetic drug (furfuryltrimethylammonium iodide) which stimulates sweat glands whose nerve supply is intact but does not affect the denervated ones.

SUBJECTS

Traumatic injuries of peripheral nerves due to gunshot or shrapnel wounds formed the bulk of our clinical material. Other conditions studied were ruptured intervertebral discs, fracture dislocation of the spine, sympathectomies and hysterical anaesthesias. A summary of the cases studied is shown in Table I.

TABLE I

Summary of cases

Peripheral Nerve Lesions	No.
Ulnar	6
Median	7
Radial	3
Sciatic	5
Common peroneal	4
Trigeminal	2
Ruptured Intervertebral Discs	3
Fracture Dislocation of the Spine	4
Sympathectomies	3
Hysterical anaesthesia	2
Total	39

The duration of peripheral nerve injuries varied between one month and two years. The patients studied were largely service personnel at the Montreal Neurological Institute, the Royal Canadian Naval Hospital, Halifax, and at the St. Annes Military Hospital.

The resistance of the central toe pads of the hind feet of 6 cats was studied over a period of 85 days following complete section of the sciatic nerve on one side. The other side served as a control.

RESULTS

A.C. and D.C. Measurements in Animals. During the first two weeks following unilateral sciatic section the electrical skin resistance (E.S.R.) of the central toe pads of both sides was measured both for Direct Current (maximum of 50 microamperes) and for Alternating Current (60 cycles). Measurements were taken on the 2nd, 5th, 8th, 10th, and 14th postoperative days. Results of the 8th postoperative day are presented as typical of this series for comparison of A.C. and D.C. values (Table II).

TABLE II

A.C. and D.C. resistance following sciatic nerve section in the cat.

	A.C. Resistance (in megohms)		D.C. Resistance (in megohms)	
Animal	Sectioned	Control	Sectioned	Control
1	0.210	0.030	4.20	0.033
2	0.210	0.025	3.50	0.056
3	0.310	0.031	8.00	0.056
4	2.000	0.140	15.00	0.200
5	2.300	0.056	30.00	0.165
6	0.585	0.064	30.00	0.125
Average	0.936	0.058	15.12	0.106
Ratio	16		142	

It is clear that the A.C. resistances are consistently lower than the D.C. values and, what is more important for this study, the ratio of resistance in normal and denervated skin is much higher for D.C. resistance than for 60 cycle A.C. Measurements of A.C. resistance were consequently abandoned.

Course of Change in D.C. Resistance Following Sciatic Nerve Section in the Cat. On the day following section of one sciatic nerve the denervated central foot pads of the six animals showed an average increase in resistance of about 20 times over its preoperative level. It was about the same amount greater than that of the control side (2.4 megohms as compared to 0.112 megohms). The resistance of the control side varied between 0.100 and 0.275 megohms throughout the 85 days the animals were studied. On the 4th day there was a further slight increase in resistance of the denervated skin, while on the 8th day it had reached 15 megohms and continued to increase to 38 megohms on the 13th and 20th days. The resistance then fell to about 4.5 megohms on the 35th day to rise slightly to 9.7 on the 85th day. These changes are shown in Fig. 2.

These observations confirm the results of Richter[2,4] and Tower and Richter[12,13,14] following sympathectomy in animals, namely that there is an initial moderate rise in resistance of the denervated skin followed by an increase in resistance to an extremely high level. The initial rise is probably due to the interruption of reflex innervation of the sweat glands. The extreme rise probably represents complete denervation and absence of autogenous function. The subsequent fall in resistance to a constant lower level, which is still many times greater than that of the normal skin, probably represents some

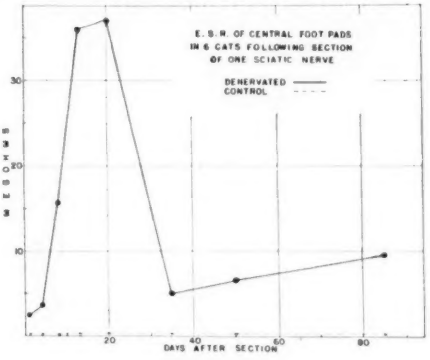

FIG. 2.

return in sweat gland function due to a form of autogenous innervation, possibly on a humoral basis.

Loss of sensation in the foot pad accompanied the elevated skin resistance and persisted until the final measurement on the 85th day.

CLINICAL STUDIES

It was in the peripheral nerve lesions that the best results were obtained and seemed to be of most practical value. If the lesion was distal to the point where the sympathetic fibres joined the nerve, then the area supplied by that nerve showed a great increase in resistance. There was a sharp line of demarcation between the denervated and normal areas. If the nerve section was proximal to the point where the sympathetic fibres joined the nerve there was no change. This was illustrated in a patient who had had a posterior rhizotomy of the trigeminal nerve. There was a sensory loss, but no change in the E.S.R. Another patient had had a depressed fracture of the zygoma which severed the infraorbital nerve. This man showed a marked increase in E.S.R. which corresponded with the sensory changes.

Two typical cases of ruptured intervertebral disc at L_5 and S_1, with definite sensory changes corresponding to the dermatomes, were tested. There was no change in E.S.R. This again is what one would expect, as the sympathetic fibres have not as yet joined the nerve, whereas in lesions of the sciatic in the thigh there was a very marked increase in E.S.R. corresponding to the skin area supplied by that nerve.

In all but two of the 27 patients with peripheral nerve injuries the area of high resistance coincided with the area of sensory loss to within $\frac{1}{4}$ to $\frac{1}{8}$ of an inch. Discrepancies occasionally found between the E.S.R. and sensory examination were later found to be due to inaccuracies of the latter.

The *first exception* was M.L., a soldier who had received a shrapnel wound of the thigh 10 months previously. The sciatic nerve was not sectioned by the original injury, but shortly following there developed a haemorrhage in his cast which resulted in a profound ischaemia of the entire leg. When the cast was removed there was complete loss of sensation below the knee. When examined about 10 months later he showed an area of sensory loss corresponding roughly to that supplied by the deep and superficial peroneal nerves, although there were additional areas of sensory loss which did not correspond to any specific nerve lesion insofar as could be determined. The area between the first and second toes on the dorsal surface showed complete anaesthesia but a low skin resistance. There was a sharp line of demarcation between this area and the surrounding high resistance area. In other words, there was sensory loss without increased skin resistance. As this was a complicated lesion, it is quite possible that the sympathetic fibres were either intact or had recovered while the sensory fibres were still not functioning.

The *second exception* was H.T., a soldier who sustained a partial lesion of the radial and ulnar nerves. In the area supplied by the ulnar nerve there was analgesia without loss of touch sensation, and this area showed a definitely increased E.S.R. There was also analgesia without loss of touch in the skin area supplied by the radial nerve, but a portion of this area, between the 1st and 2nd metacarpals, showed a decreased E.S.R.

In partial nerve lesions this decrease in resistance in areas of sensory loss had been considered to represent an irritative lesion of the sympathetic fibres.[15]

In partial nerve lesions with causalgia the affected skin area showed an abnormally low resistance, even when compared with the homologous area of the normal limb.

None of the cases in this series could be followed long enough to evaluate the use of this method in the estimation of regeneration. The results of our examinations would have been of more definite value in many cases if they could have been compared with earlier ones. This may be illustrated by the case of W.F., whose right median nerve was injured on January 1, 1944. Skin resistance examination 10 months later showed only a slightly increased resistance in the median palm area with a gradually increasing resistance to a high level at the tips of the fingers. This observation on one examination indicates either a partial lesion or beginning recovery. An earlier examination for comparison would have helped in deciding whether re-exploration was necessary.

Two cases of hysterical anaesthesia were examined and no skin resistance changes were found over the presumably involved areas.

Four cases of transverse lesion of the spinal cord were studied and confirmed the findings of Richter and Shaw.[7] It was noted that the areas of high resistance, or sympathetic levels, did not always coincide with the sensory levels. Artificial diaphoresis was necessary to bring out clear lines of demarcation in all of these patients, since all skin areas showed a uniformly high resistance without this stimulation of sweat gland activity. Observations on three cases of postoperative sympathectomies were similar to those described

by Richter,[3] Smithwick,[11] and Richter and Levine.[6] In two cases the findings were shown to coincide with those obtained by the starch-iodine test of Minor. Again artificial diaphoresis was necessary to bring out the true differences, and furmethide proved very helpful.

Furmethide provided by far the most satisfactory means of artificial

FIG. 3. Showing area of increased E.S.R. on L.M., wounded in January 1944 at Ortona. A through-and-through shrapnel wound passing medial to the femur and severing the sciatic nerve. These tests were made 10 months later.

diaphoresis. It was effective in about five minutes following subcutaneous injections of 2 to 5 milligrams. Sweat gland activity in normal skin areas was increased, often with visible perspiration and pilomotor activity, while denervated areas were unaffected. No serious side effects were encountered. Most patients expressed an urgent desire to void. One patient showed an erythematous eruption limited to a partially denervated area on the back of his forearm. It was of interest that the E.S.R. remained very high in this denervated area in spite of the marked erythema. The local erythema was probably due to the absence of sympathetic vasoconstrictor effects, allowing an exaggerated response to the parasympathomimetic drug.

CONCLUSIONS

1. Denervated skin shows a marked increase in electrical resistance a few minutes following nerve section and remains at a relatively high level until neurotization takes place. It can be demonstrated more clearly when the sweat glands of surrounding areas are active. In the cat there is an extreme rise in resistance during the second and third week following denervation, after which it falls to a steady level, still many times higher than that of the normal skin.

2. Richter's skin resistance method is an objective, practical, and precise

test for the diagnosis of peripheral nerve injuries involving the sympathetic supply to the skin.

3. Furmethide is a simple, effective and rapid diaphoretic agent for skin resistance tests and eliminates the necessity of other time-consuming and cumbersome procedures.

4. The new dermohmmeter has made possible the testing of more patients without artificial diaphoresis. It is simple and "fool proof" in operation and enables one to make quantitative measurements of skin resistance when desired.

5. The interpretation of the results of clinical skin resistance examinations would be greatly facilitated if previous examinations, made shortly after injury, were available for comparison.

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PRIMARY CHRONIC COCCIDIOIDAL MENINGITIS A DIAGNOSTIC NEUROSURGICAL PROBLEM

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SINCE Wernicke[29] and Posadas'[16] case of coccidioidal granuloma affecting a Brazilian soldier was reported from Argentina in 1892, much more has been learned concerning this interesting fungus infection, most of it from studies of infections occurring in the San Joaquin Valley of California.

The first case in California was described by Rixford[19] in 1894, and this together with a second case observed that same year by Thorne[28] and Rixford[20] were subsequently reported in greater detail by Rixford and Gilchrist[21] in 1896. It was their impression that the organism was a protozoan belonging to the group of coccidia and they gave it the name Coccidioides immitis.

During their observation of another case, Ophüls and Moffitt[14] found the parasite grew readily on artificial media and developed a mold, belonging to the group Oidia. Subsequently, Ophüls[13] gave the name of Oidium coccidioides to the organism and coccidioidal granuloma to the lesion produced by it.

Thereafter many fatal cases of the disseminated granulomatous type were reported and it was believed generally that this was the only form in which it appeared, and that it was a chronic, progressive and highly fatal entity. In 1930 Rand[17] reported two cases of coccidioidal granuloma simulating spinal cord tumor, and emphasized the similarity of the disease to tuberculosis and its frequent confusion with it.

The more common benign pulmonary disease caused by this fungus was not appreciated until its description by Gifford[8] and Dickson[5] in 1936 and 1937. Since that time other comprehensive reports on this relatively mild manifestation of the infection have been written by Faber, Smith and Dickson,[6] Smith,[23] Smith and Baker,[24] Peers, Holman, and Smith,[15] and Goldstein and Louie.[9]

It has been estimated[4] that about twenty-five per cent of those dying of the disseminated granulomatous infection have lesions of the nervous system. The cases of so-called primary chronic coccidioidal infection, in which the first or primary clinical indication of the infection is in the meninges, occur infrequently, seldom are diagnosed prior to autopsy, and often the patients are operated upon neurosurgically for suspected intracranial tumors or abscesses.

Interestingly, of the seven cases of so-called primary coccidioidal meningitis reported by Abbott and Cutler[1] five were diagnosed at autopsy; in

one an antemortem culture taken from the nose revealed the fungus and in the other a biopsy of the arachnoid obtained in a suboccipital exploration established the diagnosis. Moreover, in three cases craniotomies were performed for suspected intracranial neoplasms and in another ventriculography for the same purpose.

In 1939 Storts[26] also reported a case of coccidioidal granuloma simulating a brain tumor in a child of four years.

The same diagnostic problem has been encountered with torula or Cryptococcus hominis meningitis. The first two cases of torula reported by Stoddard and Cutler[25] were from Dr. Harvey Cushing's service at the Peter Bent Brigham Hospital.

As mentioned by Cushing, in a discussion of a paper by Shapiro and Neal,[22] in both there were symptoms of intracranial pressure without localizing features, operation was without avail and the diagnosis was made only at autopsy. In one of the cases reported by Reeves, Butt, and Hammack[18] an operation had been performed elsewhere for a suspected right frontal lobe abscess, and recently Swanson and Smith[27] described two patients with granuloma simulating cranial tumor, one of whom was operated upon.

Because of the clinical similarity of torula and primary chronic coccidioidal meningitis, their rarity, and the differential diagnostic problems involved, it was believed sufficiently important to emphasize the diagnostic, clinical and pathologic features of the two, and to report an additional informative case of primary chronic coccidioidal meningitis.

REPORT OF CASE

History. A 37-year-old soldier was well until 26 July 1943, when he contracted a respiratory infection with fever persisting for three days. He then improved until the evening of 1 August, when he fainted. Following this, his wife observed that he talked incoherently and was confused. That evening he was admitted to the West Los Angeles Area Station Hospital, where he was described as being drowsy, incoherent, and confused.

The following morning his symptoms subsided and during the ensuing week he was so much improved he was about to be discharged, when he developed a slight fever and again became confused and lethargic. A spinal puncture at this time revealed 690 cells with 13 per cent polymorphonuclear cells and 87 per cent lymphocytes, a sugar of 25 mg. per cent, and a four plus Pandy. A stiff neck and a positive Kernig were found on examination and a repeated spinal puncture disclosed opalescent spinal fluid under slightly increased pressure with 890 cells, of which 80 per cent were lymphocytes. The sugar was 32 mg. per cent and the Pandy four plus. No growth was obtained on the blood or spinal fluid cultures. He was given sulfadiazine for eleven days. Unfortunately no chest roentgenogram was taken during this hospitalization. In about three days the meningeal signs disappeared, but a left positive Babinski sign was noted. A spinal puncture performed 23 August 1943 showed 420 cells which included 2 per cent polymorphonuclears, 68 per cent lymphocytes and 30 per cent large monocytes, with a sugar of 46 mg. per cent and a four plus Pandy. The culture revealed no growth. In view of the fact that he continued to complain of headache, and because of his history and clinical findings, he was transferred to the Hoff General Hospital 25 August 1943 with the impression that he had a right frontal lobe abscess.

Clinical Findings and Course at Hoff General Hospital. On admission the patient was alert, responsive and cooperative. His temperature was 99.6 degrees by mouth, urinalysis was normal, and the blood count disclosed 4,670,000 erythrocytes, 9,900 leukocytes, and a hemo-

globin of 12.1 gm. per cent. The differential count showed 74 per cent polymorphonuclear cells, 24 per cent lymphocytes, 6 per cent monocytes and 2 per cent eosinophiles. He complained of mild frontal headaches. There was no evidence of stiffness of the neck, nor a positive Kernig sign. With the exception of a slight elevation of the medial sides of both optic discs of about 0.5 diopters and a suggestive right lower facial weakness, the cranial nerves were normal. There was a slight ataxia of the left upper and lower extremities, the deep reflexes were hyperactive throughout, more marked on the left, and the Babinski reaction was positive on the left with diminished abdominal reflexes on the same side. A right frontal lobe abscess was the admission impression.

Roentgenograms of the skull 28 August 1943 revealed no evidence of sinus infection, increased pressure or other abnormalities. Moreover, the pineal was calcified and in the midline, which seemed rather incompatible with the consideration of a supratentorial space-occupying lesion. Roentgenogram of the chest 27 September 1943 showed no evidence of pathology.

During hospitalization his clinical course varied from asymptomatic periods to those in which he complained of occipito-frontal headaches, diplopia, blurred vision, nausea and vomiting. It was believed a right frontal lobe abscess or a granulomatous infection should be considered, that sufficient time had elapsed for encapsulation, and that ventriculography was indicated.

Ventriculography. On 4 October a left occipital trepanation in preparation for ventriculography was performed under local anesthesia. During the procedure the patient had a right-sided Jacksonian convulsion with a residual right hemiparesis and aphasia which persisted most of the afternoon before subsiding.

In view of this episode it was believed a left frontal lobe abscess was likely. On 6 October 1943, after unsuccessful efforts to tap the left posterior horn, a right occipital trepanation was performed followed by ventriculography. Although visualization was not complete, the left temporal horn and third ventricle failing to fill, the anterior horns were in the midline and the left slightly dilated. It was believed this excluded fairly well the possibility of a frontal lobe expanding lesion and that the findings were not sufficient to justify operative intervention at that time.

The patient tolerated the procedure without untoward effect and by 14 October he was out of bed feeling well and mentally clear. There were no localizing signs and it was believed the clinical picture was one of encephalitis. Thereafter, his behavior varied. For a week or more he would walk around the ward feeling fairly well, and then he would become confused and often would have to be brought back to his room. He would also have periods of headache and vomiting which would keep him in bed for several days before the symptoms would subside.

On 3 December 1943 another episode of vomiting and headache occurred associated with a slight weakness of the right leg. On this occasion a lumbar puncture disclosed an initial pressure of 380 mm. of spinal fluid. The cell count was 326, all lymphocytes, the Pandy was three plus and the culture revealed no growth. Another episode of projectile vomiting occurred on 5 December. Examination disclosed bilateral papilloedema and bilaterally positive Babinski signs. He failed to improve and on 27 December right homonymous hemianopsia and aphasia were demonstrable, indicating a lesion in the left occipito-parietal region. A slight inflammation of the right external auditory meatus was discovered 27 December, but was not considered contraindicative to surgical intervention and unfortunately no culture or smear was made.

A ventriculogram 29 December 1943 disclosed excellent filling with no midline ventricular shift and a slight dilatation of the left ventricle. There appeared to be some elevation of the left temporal horn, and this together with the clinical findings of right homonymous hemianopsia, aphasia, and the right-sided Jacksonian convulsive seizure described previously, seemed sufficient evidence to warrant exploration of the left parieto-occipital area. It nonetheless seemed unusual for an expanding lesion not to reveal a lateral ventricular shift.

Operation. A left occipito-parietal osteoplastic flap was reflected in the usual manner,

Prior to this, a ventricular needle was inserted in several directions through a burr hole opening in the lower anterior portion of the bone flap. No indication of an abscess was found. The dura in the posterior portion of the exposure was then opened. The cerebral tissue in the region of the posterior temporal lobe appeared softened and portions of this were resected for diagnostic purposes. Examination of the occipital and remaining portions of the temporal lobe failed to disclose anything of a pathologic nature. Portions of a thin, brownish membrane, believed indicative of absorbed blood from the first ventriculogram, were removed from the subdural region for pathologic study. No further surgical intervention seemed indicated and closure was then carried out in the usual manner.

The ventricular fluid contained 200 cells with 2 per cent polymorphonuclears and 98 per cent lymphocytes, a 2 plus Pandy and no growth was obtained on culture.

Surgical Pathology. The surgical specimen consisted of three pieces of hemorrhagic brain tissue, each measuring approximately $1.8 \times 1.5 \times 0.6$ cm., and three sheet-like pieces of yellowish-brown tinged dura, 1 to 2 mm. in thickness, which histologically revealed fibrous tissue containing numerous blood vessels and showing many fibroblasts and hemosiderin-filled macrophages. Histological studies of all of the brain tissue disclosed no evidence of neoplasm. Oligodendrocytes similar to the satellities about ganglion cells were seen surrounding a number of the capillaries in the white matter. Some variation in the number and frequency of ganglion cells was seen in different areas of the cortex. The pathologic impression was encephalitis, etiology and type undetermined.

Postoperatively a right homonymous hemianopsia and aphasia were demonstrable. Fluid collecting under the scalp flap was aspirated approximately every two days. Cultures including the use of Sabouraud's media failed to reveal any growth until 18 January when a culture of non-hemolytic staphylococcus was obtained. This disappeared 22 January under penicillin therapy by flap injection, 50,000 units being used every other day for a total of 200,000 units. The patient was also placed on sulfadiazine 29 January, but was able to continue this orally for only three days. The cell count of the aspirated fluid varied from 30 to 270, mainly lymphocytes, with a strongly positive Pandy always present. The patient failed to improve, developed a right hemiparesis and then a tetraplegia with nuchal rigidity and positive Kernig. He became worse rapidly and died on 6 February 1944, more than six months after the onset of his illness.

Comment. Diagnostically the condition was baffling and intriguing. The illness began as meningitis, which suggested a virus infection, no organisms ever being discovered but lymphocytes being numerous. He was transferred to the Hoff General Hospital with the impression of right frontal lobe abscess, which was eliminated ventriculographically. Subsequent ventriculograms disclosed an elevation of the left temporal horn with no shift in the ventricular system, which seemed unusual for a tumor, but with the right homonymous hemianopsia, the right-sided convulsive seizures and a temporary right hemiparesis, localization of a lesion to that area seemed probable. Exploration disclosed no tumor, but tissue that appeared degenerated in character. The surgical pathologic impression was that of encephalitis, type and cause not determined. His subsequent course with right hemiparesis, aphasia and tetraplegia, as well as the continued lymphocytic response and the papilloedema of long duration, seemed unlike a virus encephalitis and compatible with a demyelinating condition of the central nervous system, such as encephalitis periaxialis diffusa of Schilder, and such was the antemortem diagnosis.

Autopsy. Gross Examination. The following pertinent findings were abstracted from the protocol. Reflection of the scalp uncovered two pockets of accumulated fluid between the

scalp and the bone flap containing an approximate total of 175 cc. of clear yellowish fluid. Their walls were formed by fairly thick, slightly yellowish scar tissue. The bone flap measured approximately 8 cm. and was attached by fibrous tissue. The cerebrospinal fluid was clear and the subdural space was free from adhesions except in one small circular area near the posterior-inferior margin of the bone flap, where the brain tissue was adherent to the bone. Two small burr holes were seen in the occipital region on either side of the midline. The accessory nasal sinuses, middle ears, pituitary and venous sinuses were all negative.

After removal, the brain was symmetrical except for slight irregularity of the left parietal

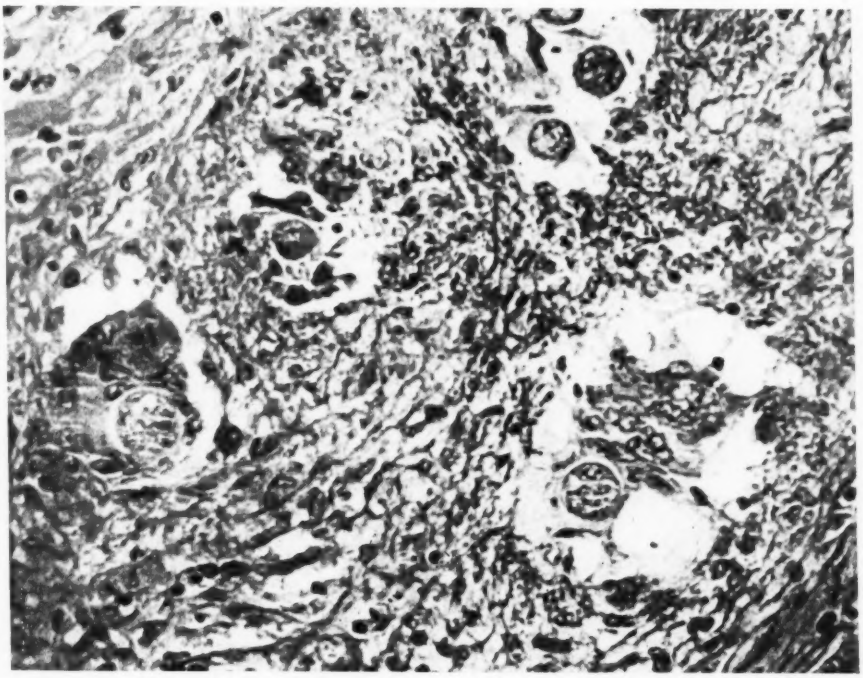

FIG. 1. Photomicrograph of a section taken through the brain stem, showing typical coccidioides spherules within multinucleated giant cells.

region, but no evidence of tumor or softening was seen in the fresh specimen. The inferior surfaces of the pons and medulla and upper portion of the spinal cord were covered by a thick layer of grayish-white exudate containing numerous small, white elevations, grossly resembling tubercles. The sulci and fissures on the inferior surface of the cerebrum were filled with similar exudate. Sectioning the cerebrum disclosed essentially normal-sized lateral ventricles with moderate dilatation of the third ventricle. The operative area was the site of a small cyst measuring $2 \times 1.5 \times 1$ cm., containing light brown fluid. Its wall was soft and light brown in color for a thickness of 2–5 mm. Sections of the cerebellum, pons and medulla showed the layer of exudate on their inferior surfaces to measure 1–3 mm. in thickness. Except for diffuse atelectasis in the posterior half of the lower lobes of both lungs, gross examination failed to disclose anything of significance.

Microscopic Examination. Sections from the brain stem and base of the cerebrum showed a thick layer of gray exudate thickening the meninges, in which were many granulomatous areas composed of epithelioid cells, fibroblasts and macrophages, with infiltration by round cells and polymorphonuclear leukocytes. Throughout the inflammatory tissues were seen many large, bizarre-shaped multinucleated giant cells, within which were located typical coccidioides spherules composed of a peripheral hyalinized capsule and a central granular area in which occasionally endospores were seen. Many spherules were scattered diffusely in the exudate (Figs. 1 and 2). Extension of the inflammatory process into the brain substance

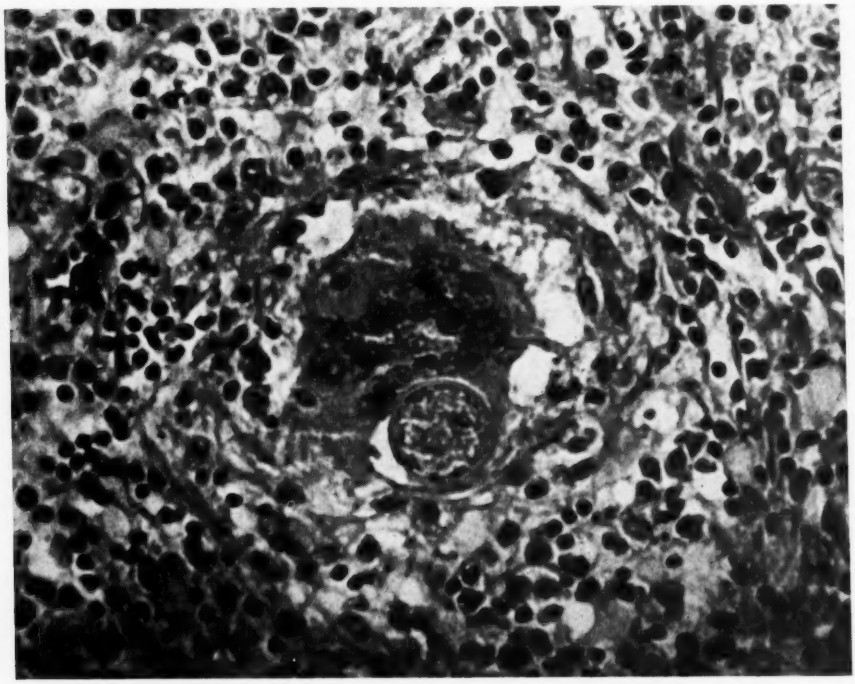

FIG. 2. Photomicrograph of a section taken through the base of the cerebrum, showing a typical coccidioides spherule within a large multinucleated giant cell.

was not seen. The meninges over the vertex of the cerebrum were infiltrated with a few hemosiderin-filled macrophages. The ganglion cells in the pons were reduced in number and some of them demonstrated chromatolysis to a marked degree. A few of the blood vessels in the pons were cuffed by round cell infiltration. The tissue at the site of operation revealed extensive glial proliferation and infiltration by round cells and macrophages, some of which contained hemosiderin. There was some fibroblastic proliferation in the wall of the small cyst. Routine microscopic examination of all of the visceral organs revealed no evidence of coccidioides granuloma.

Bacteriological Examination. Postmortem cultures of the material taken from the base of the brain produced typical growth of coccidioides mycosis. Cultures of the spinal and ventricular fluid and from the scalp flap during life were made on Sabouraud's medium because of the possibility of torula meningitis, but no growth of coccidioides was ever obtained.

DIAGNOSIS AND CLINICAL PICTURE

As was emphasized previously, not only may the antemortem diagnosis of so-called primary coccidioidal meningitis be difficult, but rarely is it made, and frequently because of the protean nature of its clinical manifestations neurosurgical operations for a suspected cerebral abscess or tumor are performed. Similar diagnositic difficulties have been experienced with torula or C. hominis meningitis.

Because of the similarities of the clinical picture, consideration of the differentiating features of the fungi comprising the blastomycetes must be emphasized. In this group, cryptococcosis or torula infection, blastomycosis or oidomycosis, and coccidioidal granuloma are those most apt to be confused. Differentiation must be made by means of morphologic characteristics, cultural reactions, and animal inoculation of the spinal fluid, in which instance, when growth is obtained, the identity can be established with certainty.

Naturally chest roentgenograms may lead to the impression of coccidioides. A positive coccidioidin skin test is evidence of a past or present infection, and this in the presence of an elevated sedimentation rate is highly indicative of active infection. Coccidioidin serologic tests have been additionally helpful. Precipitin and complement fixation tests usually are negative in the mild infections, while precipitins are present in high dilutions in severe infections, with the titer of complement fixation directly proportional to the degree of coccidioidal involvement. Similar reactions can be expected with torula and oidia. In obscure cases of meningitis, much as described in the present report, the importance of such tests is obvious, but such fungus infections are so relatively uncommon that tests of this sort are often overlooked.

The importance of spinal fluid culture in such cases is also obvious, but unfortunately even after repeated culture no growth may be present, especially in coccidioides.

From the standpoint of neurosurgical intervention, ventriculography should eliminate many craniotomies, but some of the granulomas associated with surrounding edema will continue to be misleading.

MORPHOLOGIC AND CULTURAL CHARACTERISTICS

Morphology. Compared with ordinary bacteria, the fungi of these three diseases are all of very large size. Coccidioides immitis, the largest, varies from 5 to 80 microns. In tissue or pus from inoculated guinea pigs, the cells are rounded or spherical, and multiply only by endosporulation, large numbers of small bodies escaping from the ruptured capsule of the parent organism. Two types of rupturing cells may be seen. Those of 20 to 30 microns are filled with minute particles which develop a visible wall when discharged and come to resemble the parent cell, while the larger cells, 40 or more microns in diameter, are covered frequently with radial spines. These con-

tain many spore-like bodies which increase in diameter to 4 or 5 microns and acquire a visible double-contoured wall while still in the mother cell.

In the patient's lesions and in those of inoculated animals, the round or oval cells of blastomycosis vary from 4 to 20 microns in diameter. They are rather refractile bodies containing granules of various sizes and often vacuoles, and are surrounded by a capsular-like membrane. In contrast to the coccidioides, like yeasts, multiplication occurs only by budding.

The cells of the pathogenic torula are less uniformly round and smaller than those of the blastomyces, measuring 1 to 13 microns in diameter. Budding, which constitutes their only method of reproduction, is invariably evident, the buds having thinner walls than the mother cell, whose walls may be highly refractile. Surrounding the organism in the tissues there is practically always a clear zone composed of gelatinous material, which constitutes a characteristic feature of the lesion, and which caused Stoddard and Cutler to name the parasite Torula histolytica. The organism itself is surrounded by a thick capsule of mucoid material.

Cultural Characteristics. These three pathogenic micro-organisms grow fairly readily on the ordinary nutrient media, but with the oidium (blastomyces) and coccidioides the form of growth is entirely different from that in the tissues, appearing here as a luxuriant mass of long, branching mycelia, much like ordinary molds. With torula, however, the form of artificial growth is practically identical with that in the tissues, having no resemblance to molds and consisting of yeast-like budding organisms.

The cultural characteristics of these three fungi also reveal differentiating features. The mucoid consistency of the growth of C. hominis is a striking characteristic. Gelatin shows only slight liquefaction after 6 to 8 weeks and no gaseous fermentation of the sugar occurs. On the various agar mediums containing sugar, the fungus produces a moist cream-colored growth which often becomes yellow or darkened with age. On maltose agar the colony assumes a deep brown pigment. In culture, moreover, coccidioides forms a branching mycelium with few septums and, in contra-distinction to oidium, forms no buds or conidia.

Depending upon the medium employed, the incubation temperature, and frequency of transplant, oidium may assume a variety of forms. It grows but feebly on nutrient agar without sugar. No fermentation of gas occurs in the sugar media, but both gelatin and blood serum are liquefied. On Sabouraud's maltose agar and similar media, the fungus slowly forms a downy or fluffy colony with abundant aerial mycelium, at first white, but often later a deep cream or tan. The most characteristic feature of the culture growth of oidium is the formation of conidia, appearing anywhere along the side of the hypae or the tips of the short lateral branches, as knob-like projections which gradually enlarge.

Coccidioides immitis resembles the various types of growth observed in Oidium dermatitidis, but usually develops an abundant, grayish-white cottony, aerial mycelium. On Sabouraud's honey agar, however, it produces a

greenish-black pigment, and a black pigment on mannitol agar which Castellani[3] regarded as a differentiating point from Oidium dermatitidis. No gas formation occurs in the sugars, but a rapid liquefaction of gelatin takes place.

PATHOGENICITY FOR LABORATORY ANIMALS

Diagnostically the difference in pathogenicity of these fungi for laboratory animals is important. Cryptococcus hominis, for example, is quite pathogenic for mice, rats, and monkeys, while rabbits, guinea pigs, and dogs have been found only slightly susceptible. Intraperitoneal injections into rats, mice, and monkeys result in lesions involving the meninges, brain, lungs, liver, and spleen, with the peritoneum but slightly affected.

Oidium dermatitidis has been found but slightly pathogenic for all experimental animals, with dogs and monkeys the most susceptible. In contrast to C. hominis, intraperitoneal inoculation produces a markedly local peritoneal reaction, and while other organs may be involved, the central nervous system has usually been spared. The gonads have been found to be the organs most susceptible to the infection and because of their accessibility constitute the most desirable part for the purpose of diagnostic inoculation.

All laboratory animals are more or less susceptible to C. immitis, rabbits and guinea pigs particularly so on intraperitoneal or subcutaneous inoculation. Guinea pig inoculation usually results in a systemic generalized coccidioidal infection and death of the animal. Intraperitoneal guinea pig inoculation with oidium, on the other hand, results in no harm to the animal and autopsy reveals no evidence of infection.

PATHOGENESIS

There is fairly good evidence that C. immitis exists in the dust in endemic areas and in most cases infection takes place through the lungs by inhalation. Infection through breaks in the skin of course can occur. The portal of entry for all three of these fungous infections can be considered similar.

PATHOLOGY

Tissues Affected. The pathologic picture produced by these three organisms is that observed in the tissues of infectious granulomas generally and the similarity to tuberculosis is striking in all three. C. hominis or torula has a predilection for the central nervous system and the lungs, involving the viscera much less frequently. The skin and skeletal systems have rarely been affected, differing in this respect from its two related diseases.

Although in blastomycosis the lesions may involve all organs, the skin and bones are usually affected. The cutaneous blastomycosis without systemic involvement usually runs a benign course and recovery with complete involution of the skin lesions eventually ensues. Blastomycotic invasion of the cerebrospinal system occurs with a fair degree of frequency in the generalized systemic type of the disease as a secondary metastatic process, and frequently there is an associated destructive osteomyelitis of the skull or

vertebral column. The skin, moreover, has been found affected, either primarily or secondarily, in 95 per cent of all recorded cases.

Coccidioidal granuloma resembles blastomycosis more closely than cryptococcosis in that cutaneous and osseous manifestations are common. The cutaneous lesions of blastomycosis are slower in evolution than those of coccidioidal granuloma, while glandular involvement, common in coccidioides, is usually absent in blastomycosis. From the standpoint of the pulmonary lesions, Carter[2] found mediastinal involvement a very frequent occurrence in coccidioides, and much less frequent in tuberculosis or blastomycosis. Ophüls[12] almost always found a pulmonary focus at autopsy and was of the opinion that the majority of cases of coccidioides originated as respiratory infections. Carter,[2] moreover, observed that radiographic studies of the chest in the early stages of the disease, regardless of the clinical picture, always revealed evidence of pulmonary pathology.

Pathologic Picture. C. Hominis. Torula infection of C. hominis results in a defensive cellular reaction similar to that observed in the tissues of infectious granulomas generally. The lesions consist of small nodules or tubercles varying from 0.5 to 8 mm. in size. As the tissue is invaded by the fungus, it becomes dissolved and replaced by the parasites and their covering of mucinous material, with a surprising lack of inflammatory reaction. Microscopically the structure of the nodules is that of miliary tubercles, composed of giant, epithelioid, and lymphoid cells with an almost total absence of polymorphonuclear leukocytes. The torula organisms may or may not be visible in the lesions, but when observed are either intra- or extracellular. The cerebrospinal picture usually consists of a diffuse granulomatous meningitis, areas of perivascular infiltration and more deeply situated embolic lesions with considerable variation in the degree of cellular reaction.[7,11] Stoddard and Cutler[25] and Freeman[7] have also noted degenerative changes in the ganglion cells with increased neuroglial formation and myelin sheath degeneration.

Oidium (Blastomyces). According to Jacobson,[10] the gross appearance of the lesions caused by oidium in tissues other than the skin may so closely resemble those of tubercle bacilli that they have been thus mistakenly diagnosed until the parasites have been discovered later in the stained sections. The gross and microscopic pathology of cerebrospinal blastomycosis has not been found to differ materially from the reactions noted in other tissues of the body. Although the organisms are most commonly found within the giant cells, less frequently they may be distributed loosely in the granulation tissues. Sometimes the fungi may be sufficiently numerous to constitute the predominating elements in the field, while on other occasions persistent search may fail to reveal the presence of a single organism.

Coccidioides. The tissue reaction to C. immitis, in all essentials similar to that observed in other infectious granulomata, includes marked proliferation of the various cell types, formation of new blood vessels, tubercles, caseation, and liquefactive necrosis with or without resultant abscesses and cavitation, and finally fibrosis and calcification.

Courville and Abbott[4] have found that coccidioides may be productive

of a rather wide variety of leptomeningeal lesions including among them, tubercles, diffuse or patchy granulation tissue, intracisternal abscess, and basal or spinal subarachnoid granuloma. The tubercles are usually observed over the dorsolateral surface of the brain, differing from those of tuberculosis in being more flattened, larger in size, and having more irregular margins. Between the tubercles and situated along the superficial vessels may be found irregular patches of exudate more characteristic of this disease than of other forms of granulomatous meningitis. Lesions within the nervous tissue rarely occur, but when observed consist usually of small, circumscribed somewhat irregular accumulations of granulation tissue. Such granulations may be discovered in the cerebral centrum or central nuclear masses and also in the cortex. Courville and Abbott have described small punched-out lesions of the skull more commonly affecting the inner table than the outer, which they believe quite characteristic of coccidioides.

COMMENT

Although no coccidioidin skin test was performed, such a fungous infection was unsuspected and, because of its infrequency, undoubtedly similar cases will remain undiagnosed prior to autopsy. In cases of obscure nonpyogenic meningitis the importance of such skin tests is obvious.

Because torula meningitis was suspected as a possibility, the spinal fluid, ventricular fluid and fluid aspirated from the scalp flap were cultured repeatedly without growth of the fungus, an occurrence not uncommonly experienced. Unfortunately no chest x-ray was taken during the patient's initial hospitalization and that taken at this hospital revealed nothing unusual. Had a smear and culture been taken from the inflammation of the right external auditory meatus, the nature of the infection might have been disclosed, much as was done in one of the cases reported by Abbott and Cutler.

The importance of emphasizing the clinical similarity between torula or C. hominis meningitis and coccidioidal meningitis of the so-called primary variety and the differential diagnostic points between the two likewise seems evident and important.

SUMMARY AND CONCLUSIONS

Not only may the antemortem diagnosis of so-called primary coccidioidal meningitis be difficult, but it is rarely made, and frequently because of the protean nature of its clinical manifestations, neurosurgical operations for a suspected cerebral abscess or tumor are performed.

The similarity of Coccidioidis immitis to Cryptococcus hominis and Blastomyces dermatitidis requires differentiation of these fungi by means of morphology, cultural reaction and animal inoculation, in which case the identity can be established with certainty. The methods of distinguishing these three fungi are discussed as well as the differences in their pathologic picture.

While all proven cases of central nervous system involvement have invariably progressed to a fatal termination, there is reason to suspect that some may have recovered and have been undiagnosed.

As in torula meningitis, the noticeable variation in the duration of the disease must be related in some way to a difference in the general resistance of the host as well as to a variation in the virulence of the fungus.

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THE USE OF TANTALUM FOIL IN THE SUBDURAL SPACE

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THE NEUROSURGICAL management of wounds of the central and peripheral nervous system sustained in modern warfare has been considerably facilitated by the introduction of tantalum. Its physical properties and inertness when in contact with body tissues have allowed its application in numerous forms, viz. plate, foil, wire and ribbon. Utilizing these different preparations, it has been possible to successfully repair cranial defects, secure hemostasis, perform accurate nerve suture and prevent postoperative adhesions (subdurally to avoid meningocerebral cicatrices; in the vicinity of peripheral nerve anastomoses and neurolyses; and extradurally in the spinal canal following disc surgery). In this communication, we are particularly interested in reporting our experiences following the use of tantalum foil subdurally in the prevention of post-traumatic and postoperative sequelae.

The high incidence of convulsions following gunshot wounds of the head with dural penetration is well known. Many of these are undoubtedly due to the formation of a meningocerebral cicatrix. Prevention of the latter, therefore, is of extreme practical importance. Pudenz and Odom[3] have recently reviewed the literature and presented their experimental results on the various materials that are available for this purpose. These included the resorbable membranes (amnioplastin, Cargile and insultoic membranes, films of 5 per cent polyvinyl alcohol) and tantalum foil. The latter, particularly, evoked only a very minimal connective-tissue and inflammatory reaction with only slight encapsulation. Attachment was noted only along the margins of the capsule. These observations were made from a study of six experimental animals over a period of from 10 to 143 days.

Delarue, Linell and McKenzie,[1] on the contrary, do not advise the use of foil subdurally in head injuries with cortical damage on the basis of a similar experimental study. In all twelve animals, thickening of the dura overlying the tantalum was found in periods of from 16 days to four and a half months following implantation. The arachnoid showed similar but less marked reactions. Early encapsulation of this material, however, was not seen until three and a half months in two animals. This process was so marked in three additional dogs that adhesions bound the foil to the subjacent cortex.

Our experiences in man in this respect have corroborated the findings of Pudenz and Odom,[3] rather than Delarue, Linell and McKenzie.[1]

Ingraham and Bailey[2] have recently introduced fibrin film as a dural substitute. Ten experimental animals were sacrificed from 24 hours to 6 months following its use. Only minimal tissue reactions were observed and the sub-

dural space was preserved throughout. The final result was the replacement of the film with a thin layer of fibrous tissue. It was further used clinically in 44 instances. Eighteen were removed for further study at periods varying from 14 hours to 81 days after implantation and the previous results were corroborated.

We have been able to observe the effects of tantalum foil when placed immediately over the cortex in six patients. The intervals between the first and second operations were 6, 21, 26, 31, 54 and 113 days. In each instance, the findings were invariably similar in all respects. A fine, thin, smooth, glistening, diaphanous membrane surrounded the foil. This envelope was very loosely adherent to the arachnoid and dura but was easily separated. No thickening of the arachnoid was seen. The cerebrospinal fluid pathways remained intact, and the subjacent cortex appeared smooth and glistening, with xanthochromia where previous contusion was present. The dura showed minimal thickening. However, in patients where the dura had been incised at previous operations, this reaction was particularly marked even when no substitute was employed. The foil showed no evidence of corrosion. Nor was there any evidence of adhesions of the encapsulated foil to the underlying cortex as mentioned by Delarue, Linell and McKenzie.[1]

CASE REPORTS

Case 1.

Skull Pathology. Depressed fracture, squamous portion of left temporal bone.

Mode of Injury. Patient was struck over the left temporal region by a pitched baseball on 30 August 1942.

Associated Injuries. Patient was unconscious for several hours. Spinal fluid was grossly bloody but under normal pressure. There was transient motor dysphasia.

Operation I. Debridement with removal of depressed bone fragments, including spicules penetrating the dura and cortex, was performed on 24 October 1942. A segment of tantalum foil was placed over the cortical laceration and the dura repaired. A first-stage tantalum cranioplasty was then accomplished. [At present, the entire procedure is completed in one stage.]

Course. Convalescence was uneventful.

Operation II. A second-stage cranioplasty was completed 54 days later, on 17 December 1942. The tantalum foil was inspected and removed for study. It was found to be enveloped by a thin, diaphanous, translucent membrane. This was easily separated from the overlying dura and subjacent arachnoid, leaving the adjacent surfaces of these membranes smooth and glistening. The arachnoid had completely healed over the cortical laceration, and the site of the original injury to this membrane and the cortex could not be localized grossly. However, the cortex for some distance surrounding this area was yellowish and appeared to be that characteristic of traumatized brain but not necessarily related to the presence of tantalum foil. The dura was then sutured and tantalum plate inserted.

Course. The patient had an uneventful postoperative convalescence.

Microscopic Examination. The membrane removed consisted of a loose, wavy, fibrous tissue. There was no significant chronic inflammatory or foreign body reaction.

Case 2.

Skull Pathology. Compound, comminuted, depressed fracture, mastoid and squamous portions of the left temporal bone.

Mode of Injury. Patient's injuries were incurred in a truck accident on 26 March 1944.

Associated Injuries. Patient was unconscious for 48 hours. There were compound, comminuted fractures of the left humerus, radius and ulna, all at the junction of the middle and distal thirds of the bones. There were similar fractures at the bases of the fourth and fifth left metacarpal bones. There was a pronounced sensory dysphasia with agraphia and acoustic and visual verbal agnosia.

Operation I. Debridement and removal of bone fragments over an area $2 \times 4 \times 5$ cm. was performed on 27 March 1944. The mastoid cells were involved. There was dural laceration and extensive laceration and contusion of the underlying cortex. A section of tantalum foil was left in the subdural position.

Course. There was marked improvement in the previous dysphasia. Electroencephalogram showed considerable delta activity over the left motor area and frequent spikes over the left occipital region. Much fast, irregular activity was seen over the entire left cerebral hemisphere. Encephalogram on 29 June 1944 showed moderate internal hydrocephalus, more evident on the left, and more particularly of the temporal horn. Patient had a series of generalized convulsions on the 4th and 5th of July.

Operation II. A tantalum cranioplasty was performed 113 days after the initial operation, on 18 July 1944. The dura was intact and only slightly thickened. The foil had crumpled and was covered with a thin film of tissue which was easily removed. The subjacent cortex was completely free from adhesions. The areas not covered by the tantalum were involved in a definite meningocerebral cicatrix which was separated with little difficulty. The brain showed evidence of previous contusion and laceration. A piece of tantalum foil was again inserted subdurally and routine tantalum cranioplasty then accomplished.

Microscopic Examination. The envelope surrounding the foil was composed of connective tissue of varying density with no evidence of foreign body reaction.

Case 3.

Skull Pathology. Compound, comminuted, depressed fracture, squamous portion of left temporal bone.

Mode of Injury. Patient sustained a gunshot wound of the gutter type over the squamous portion of the left temporal bone on 5 July 1944.

Associated Injuries. Patient was unconscious for 30 minutes. There was a transient right hemiparesis, amnesic dysphasia and hyperpathia to the eighth dorsal dermatome on the right.

Operation I. On 6 July 1944, debridement and removal of bone fragments over an area 4 cm. in diameter was performed. There was laceration of both the dura and underlying cortex. A section of tantalum foil was then placed subdurally and the scalp was closed in the usual manner.

Course. This was uneventful, with subsidence of all previous symptoms. Electroencephalogram showed a slow wave focus and bursts of fast activity over the left temporal region. Encephalogram on 22 July 1944 showed very early dilatation of the left lateral ventricle.

Operation II. A routine tantalum cranioplasty was accomplished 21 days following the first operation, on 27 July 1944. The dura was not abnormally hypertrophied. There was a thin film of tissue covering the foil, both superficially and deep, and this was easily removed. There was no adherence to either the arachnoid or dura. Previous areas of cortical contusion were verified. A new segment of tantalum foil was inserted, dura closed, and tantalum plate inserted.

Course. Convalescence was uneventful.

Microscopic Examination. The tissue surrounding the foil was fairly well vascularized, loose connective tissue. No significant foreign body reaction or chronic inflammatory changes were noted.

Results obtained in the other three cases were similar to the above in all respects.

TYPES OF CASES

From 24 October 1942 to 27 September 1944 we have used tantalum foil subdurally in at least 45 recorded cases. These included: 16 cases following acute, compound, comminuted depressed skull fractures; 12 cranial defects, residual from previous debridement; 10 brain tumors; and 7 miscellaneous cases as follows: brain abscess, 2; degenerative lesions, 2; Ménière's disease, 1; arachnoiditis, 2 (one cerebellar and one lumbar).

We have also used the foil in an undetermined additional number of cases not recorded in the operative notes. It has been our routine to use tantalum beneath the dura in all cases in which a transcortical incision is employed, not only for cerebral trauma of any type but also in the removal of brain tumors.

Two patients have complained of "clicking sensations" over the involved area after the use of tantalum foil. In one the foil was applied after a suboccipital craniectomy, and in the other, after a debridement of a compound, depressed fracture over the midline involving both squamous portions of the frontal bone, before cranioplasty. Therefore, in cases in which tantalum foil is applied over the cortex, "clicking sensations" may be a frequent complaint in the presence of a cranial defect, but have not been described following cranioplasty or a routine osteoplastic flap.

CONCLUSION

Until fibrin film or some other more ideal substitute material becomes available, we feel that tantalum foil is well adapted for subdural application in the prevention of postoperative sequelae following intracranial surgery. Contrary to the experimental results of Delarue, Linell and McKenzie,[1] we have not found subdural tantalum foil associated with thickening of dura and arachnoid any more than is seen with ordinary operative procedures exposing the cortex. Many of the casualties returning from overseas theaters of operations have sustained penetrating intracranial wounds with resulting cranial defects and other evidence of neurological deficit. Cranioplasty has revealed a number with marked meningocerebral cicatrices, some having already developed epilepsy and other post-traumatic residuals, depending upon the site of injury. It is in this group, particularly during modern warfare, that the subdural use of tantalum foil would do much to obviate many of these serious sequelae.

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AN AUTOMATIC SELF-RETAINING LAMINECTOMY RETRACTOR

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IN PERFORMING a laminectomy it has been our experience that the existing self-retaining retractors do not meet the prerequisites for ease of retraction for bilateral or unilateral laminectomies. With these facts in mind a ratchet type of retractor has been designed.

Heretofore, in extremely obese people or in areas in the back where the muscles are quite thick, we have found that the blades of the existing laminectomy retractors were too short. To allow flexibility so that deep muscles could be retracted as well as shallow muscles, the blades of this retractor are removable. A blade of any length can be inserted instantly.

Undue force is necessary to separate the blades of the existing retractors by either the surgeon or his assistants. By using the ratchet device we have been able to eliminate this so that retraction may be obtained with the greatest of ease.

The prongs of the blades of the existing retractors are so designed that they will not hold *in situ*. In order to prevent this retractor from slipping out of the wound, curves have been placed at the tip of the prongs of the retractor blades.

In unilateral procedures, such as utilized for disc operations, rapid retraction can be obtained by using the muscles on one side and a spinous process on the opposite side as anchor points. The simplicity of construction makes operation quite easy and sterilization satisfactory.

In addition, this retractor principle can be used for other surgical procedures by merely designing other types of blades.

In Fig. 1 *A* and *B*, the retractor is shown as having power arms *1* and *2*. The power arm *1* is formed integral with a ratchet bar, *3*. This bar extends at right angles to the power arm *1* and its outer face is formed with ratchet teeth, *4*. A fitting, *5*, is formed integral with the arm *2* and has a passageway there through to receive the ratchet bar *3*. Operating handles, *6* and *7*, are mounted upon the members *3* and *5* respectively. A setting lever, *8*, is pivoted upon the bar *2* and carries a dog, *9*, which may engage the ratchet teeth, *4*. A suitable lock device is mounted within the member *5* to hold the ratchet bar *3* and member *5* in temporarily locked relation while a release lever, *10*, is provided to render the lock ineffective. Adjustably mounted upon the bars *1* and *2* are retractor blades *11* and *12*. It will be evident that these blades may be interchanged for particular purposes.

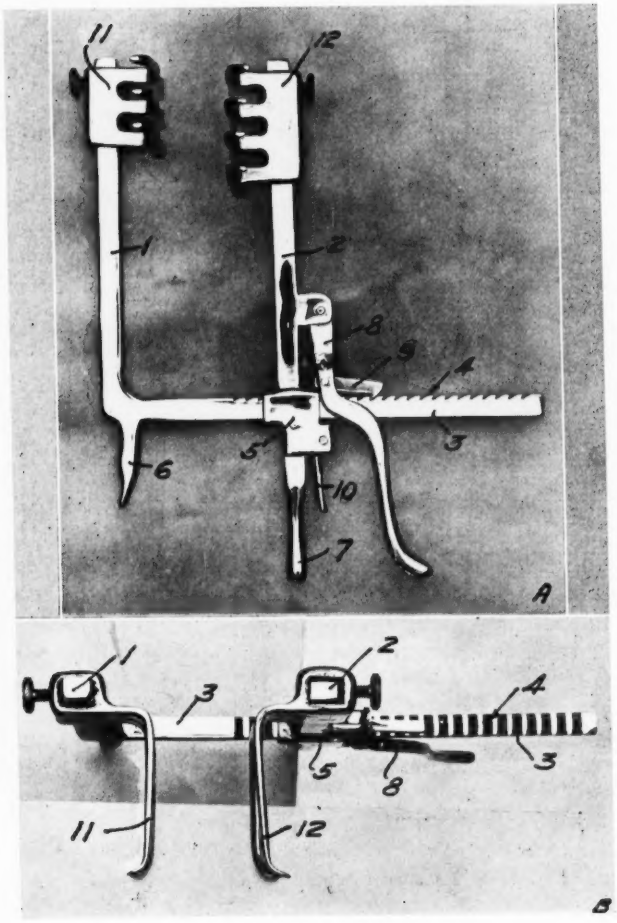

FIG. 1

CONCLUSION

This retractor* is so designed as to give wide exposure with a minimum effort and maintain this exposure throughout the entire operative procedure.

* This retractor is now available and may be purchased from the Woods Professional Supplies, 8442 Otis Street, Southgate, California. Patent applied for.

CAROTID SINUS SYNCOPE SECONDARY TO LIGATION OF CAROTID VESSELS FOR INTRACRANIAL ARTERIO-VENOUS ANEURYSM

REPORT OF A CASE WITH SURGICAL CURE. ELECTROENCEPHALOGRAPHIC AND ELECTROCARDIOGRAPHIC STUDIES

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(Received for publication February 21, 1945)

As a direct result of the present war, numerous freak injuries of the nervous system and/or the vessels directly supplying the brain and spinal cord have been observed.

The following case report is that of a soldier who received severe injuries to the head and body with the subsequent development of an intracranial arterio-venous aneurysm which was controlled by ligation of the carotid vessels. As a result of this operative procedure, which was aimed particularly towards the saving of the only remaining eye, opportunity was afforded for the study of the pathogenesis of a typical example of the syndrome of carotid sinus syncope of the cardiodepressor type. In addition, controlled serial electroencephalographic studies were carried out with some rather unusual findings.

Weiss, Ferris and co-workers[1,3] have described the three types of syncope due to sensitive carotid sinus from the clinical standpoint, as follows: (1) Cardiodepressor, in which there is an appreciable slowing of pulse rate or even asystole, without essential change in the blood pressure; (2) the vasodilator type, in which syncope is associated with fall in blood pressure; and (3) the central type, in which syncope occurs without appreciable change either in blood pressure or pulse rate. Forster, Roseman and Gibbs[2] have recently described the electroencephalographic pattern in all three types of the carotid sinus syncope syndrome. Yeager[4] was able to study the electroencephalographic pattern before and after ligation of the carotid arteries in a case of intracranial saccular aneurysm and noted large slow waves in the electroencephalogram immediately following ligation. The examples referred to above are somewhat amplified in the following case report.

REPORT OF CASE

History. H.W., a single 28-year-old private, was admitted to the Walter Reed General Hospital on 29 September 1943. His past history was irrelevant except for the fact that in 1940, while in civilian life, he was accidentally shot, during a brawl, in the right lower quadrant of his abdomen with perforation of the bowel in several places and with subsequent development of a severe peritonitis. However, he made a slow but complete recovery from this accident and was in good health until his induction in the Army on 4 September 1942. He was

sent to Africa on 26 January 1943 as a mechanic in the Air Forces and was helping in the preparations for the forthcoming Sicilian campaign. On 22 July 1943, the patient was aiding in the loading of motorcycles and jeeps into air transports. He was driving a motorcycle up a ramp to one of the transports when he struck some obstruction and both he and the motorcycle overturned in such a fashion that the patient fell on his back and the cycle struck him on his face and head. The patient stated that he was unconscious for a period of two days and was "crazy in the head" for another week. He was admitted to a general hospital within a few hours following injury where it was noted that the right eye showed a marked degree of edema and ecchymosis of the lids, with chemosis of the conjunctiva and cornea, and no light perception. There was a laceration from 10 to 1 o'clock along the corneal region with some haze under the conjunctiva. There was subcutaneous emphysema about that eye and face, and tenderness all along the zygoma and maxillary bones on the right. Fresh blood was present in both nares and in the right auricular canal. The right ear drum was perforated. The patient was unconscious and in shock. X-ray studies revealed: Fractures of the base of the skull, right mastoid process, the right ramus and condyle of the mandible, the right malar bone extending across the orbital plate and the right clavicle at the junction of the outer and middle one-thirds.

The patient began to drain cerebrospinal fluid from both ears and nares. He was treated for shock by means of whole blood, plasma, immobilization of the accessible fractures, and by the judicious use of sedation. By 24 July he was well enough to be transferred to another general hospital, at which time he was drowsy but well oriented. On 26 July a complete paralysis of the left sixth and seventh cranial nerves was noted. Hearing in both ears was markedly impaired and there was a bluish discoloration and perforation of the left ear drum. He was placed on sulfadiazine on 26 July and this drug was continued in four-gm. daily doses until 4 September. Cerebrospinal fluid continued to drain from both nostrils until 1 September 1943. By 1 September 1943 hearing in both ears had returned to normal and he was able to be up and around. His course during the first two months following injury was marked only by minor, comparatively rare, headaches. There were no other gross neurologic signs. Blood pressure was 120–130 systolic and 70–80 diastolic without much variation from these limits. The general medical examination otherwise was not remarkable.

Clinical Findings at Walter Reed General Hospital. On admission 29 September 1943 the nose and nasal accessory sinuses were found to be clear both on physical examination and by x-ray. The ear canals were normal and the drums appeared normal. Hearing in the right ear was 15/15 and in the left 12/15. Vision in the right eye was nil and in the left eye was 20/20—Jaeger-1. The visual field of the left eye was normal. The right eye showed a shrunken phthisical globe. There was paralysis of the left external rectus muscle and complete paralysis of the left face, of infranuclear type. The corneal reflex and the left fundus were normal. Lumbar puncture revealed initial pressure of 150 mm. of water, with clear colorless fluid containing no cells, negative globulin, total protein of 22 mg. per 100 cc. of spinal fluid, and negative Wassermann and colloidal gold reactions.

On or about 1 October 1943 the patient first noted a buzzing sound in his left ear. This sound was likened to a swishing noise, which was synchronous with his pulse beat, and varied in intensity from time to time, depending on his state of activity. Examination on 11 October revealed a slight proptosis of the left eye, and a definite bruit, which was synchronous with the pulse, could be heard by placing the stethoscope on the left temple and over the left eye. Obliteration of the left common carotid pulse by pressure caused immediate disappearance of the subjective noise and the objective bruit. A diagnosis of arterio-venous aneurysm of the left internal carotid artery and cavernous sinus was made. Because of the possible loss of vision in the one remaining eye, and because of the subjective noise, it was decided that ligation of the left common carotid artery was indicated.

Operation I. Following prolonged periods of digital compression of the left common carotid artery, the patient was taken to the operating room on 15 October 1943 and a preliminary tarsorrhaphy of the left eye was performed. The left common carotid artery was then exposed for a distance of about two inches. A rubber band was placed about the vessel and by

traction it could be easily occluded. This immediately stopped the buzzing sound in the patient's head and produced no untoward symptoms or signs. There was no change in blood pressure or pulse. The vessel was held occluded for thirty minutes and the patient tolerated this well. Thereupon, a tantalum band, 5 mm. in width, was placed about the common carotid artery and compressed until all pulsation distal to the band ceased. One end of this band was made to overlap the other shorter one in order to prevent expansion. Following this there was no subjective swishing sound in the head or objective bruit, and the superficial temporal pulse was obliterated. There were no abnormal neurologic signs.

Course. The postoperative course was uneventful.

Operation II. On 20 October 1943 a simple enucleation of the right eye was done. Following section of the optic nerve there was a severe gush of blood which, however, was controlled by the use of pressure packs.

Course. The postoperative course was not remarkable until 22 October 1943, when the patient again complained of the buzzing sound in his left ear. An audible bruit could not be heard. Because the subjective buzzing became more severe and proptosis again became notable, the patient was again taken to the operating room.

Operation III. On 30 October 1943, under local anesthesia, the old wound was revised. The common carotid artery at the site of previous ligation was imbedded in scar tissue. The tantalum band was exposed and found to have completely obliterated the common carotid artery. The common carotid artery was then exposed at its point of bifurcation and the internal carotid artery mobilized. The latter was compressed and the subjective noise disappeared. Ten cc. of thorotrast were then injected into the internal carotid artery, and x-rays showed an area of increased density on the left side of the sella turcica. A tantalum band was then placed about the internal carotid artery approximately 1 cm. distal to the bifurcation. Immediately all noises in the patient's head stopped.

Course. For two hours following operation the patient had a right Babinski and increased right ankle and knee jerk. He was otherwise asymptomatic.

On 4 November the patient had an intermittent buzzing in his *right* ear, which appeared from time to time but in a period of 5 or 6 months gradually became non-extant. He frequently complained of burning and tearing of the left eye and this eye on numerous occasions showed marked conjunctival injection. His course was otherwise asymptomatic until 15 December 1943. On this date he noticed that upon sudden turning of his head *to the right* his heart would skip one or two beats and he would feel faint. This was inconstant but occurred two or three times per day. On 16 January 1944 he had a focal convulsion. This came on while he was in the sitting posture and immediately after he had suddenly turned his head to the right to address another patient. He fell to the floor unconscious and had convulsive movements of his right extremities lasting for 10 seconds. He had numerous similar episodes subsequently. There was no previous history of syncope or convulsions and no family history of the same.

Operation IV. On 28 February 1944, following preliminary simultaneous electroencephalographic and electrocardiographic studies carried on during massage of the left carotid sinus, the left carotid bifurcation was excised *in toto*. The previous scar along the anterior border of the left sternocleidomastoid muscle was excised. The section was carried downward until the tantalum clip on the common carotid artery was identified. The internal and external carotid arteries were then dissected free. The tantalum clip on the internal carotid artery was seen to have completely occluded the vessel, thus demonstrating that a tantalum band was an adequate and a safe method of occluding large vessels. The dissection was carried distally along both external and internal carotid arteries. The external carotid artery was then doubly ligated and cut. The internal carotid artery distal to the tantalum clip, and an equal distance from the bifurcation, was likewise doubly ligated and sectioned. The common carotid artery was then cut, no ligature being necessary because of the previous tantalum clip. However, another clip was put on as a safeguard. The bifurcation of the common carotid, its two branches, the carotid body, surrounding nerve fibers, scar tissue and tantalum clip on the internal carotid artery, were then removed in one piece (Fig. 1). The vagus nerve and sympa-

thetic chain were identified. Because of the left facial paralysis and proptosis of the eye, and hence the inability of the patient to close his left eye (in spite of a previous Fuchs' tarsorrhaphy), the sympathetic chain was then crushed, in order to produce a Horner's syndrome.

Course. The patient made an uneventful recovery. The left eyeball was sunken and the left pupil was smaller.

Numerous plastic operations were performed on his face and eyes. The right eye socket was fitted with a well emplaced prosthesis. Several Fuchs' tarsorrhaphies were performed on the external canthus of the left eye, the last one on 19 February 1944. As a result of the latter procedure, plus the left Horner's syndrome, the patient was able to close the left eye completely. On 17 January a plastic repair of the left side of the face was carried out by a sling of tantalum wire anchored to the left temporal fascia. During October and November 1943, the

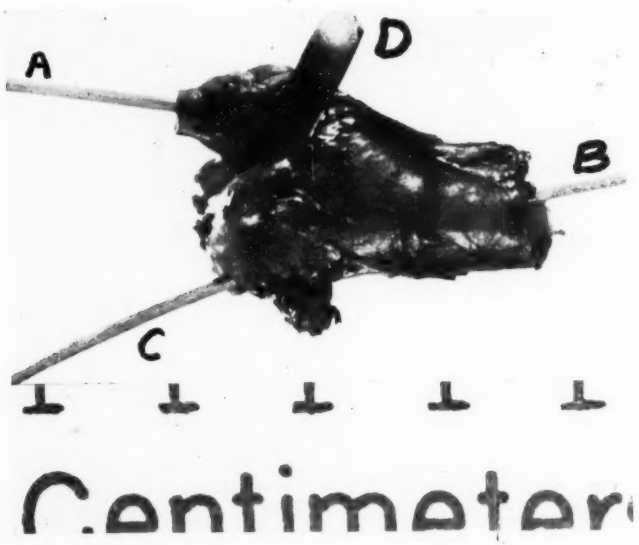


FIG. 1. Excised carotid bifurcation. (B) Common carotid artery. (C) External carotid artery. (A) Internal carotid artery. (D) Tantalum band on internal carotid artery.

fractures of the mandible were reduced and immobilized, with resultant firm consolidation at sites of fracture, with no deformity and with relatively little disability or loss of function about the jaw.

He was sent on a convalescent sick leave of thirty days starting 15 March 1944. During the entire time that he was home and subsequently until the period of observation ceased, about 1 December 1944, the patient had no further convulsions and no episodes of faintness or skipped beat. He noted, however, that his tolerance to alcohol was quite small and that he would become drunk very easily and have very marked hangovers. Accordingly, he cut down on his alcoholic intake, gained much weight, and improved both from a physical and mental standpoint.

ELECTROENCEPHALOGRAPHIC STUDIES

Numerous control tracings, beginning on 1 October 1943 (using the Grass 6-channel electroencephalograph), were obtained. A total of 55 EEGs

were made. Several control simultaneous electroencephalographic and electrocardiographic tracings were made with the patient in a recumbent posture and while alternately massaging each carotid sinus, and the clinical responses and changes in the EEG and EKG, if any, were noted. Prior to the ligation of the common carotid on 15 October 1943 there was no evidence of any slowing in the pulse rate, change in blood pressure, or in the electroencephalogram, upon massage of either carotid sinus. The control EEG tracings showed a moderately dysrhythmic record (Fig. 2). The dominant rhythm

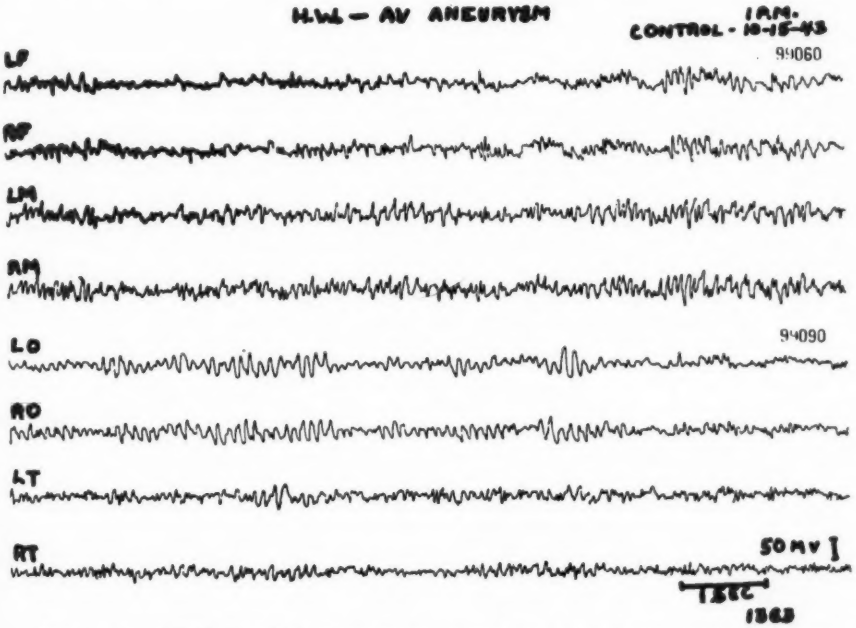
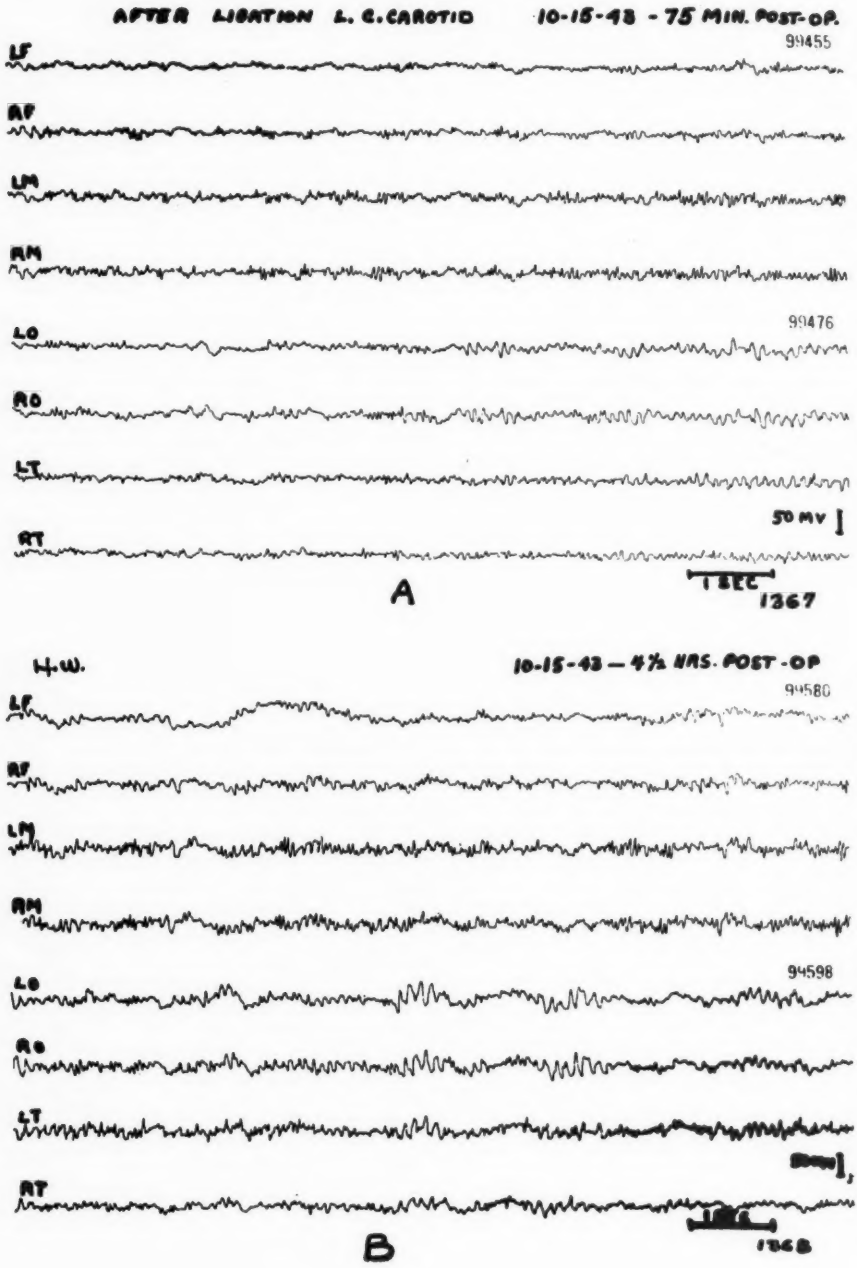


FIG. 2. Control EEG. Note high-voltage 25–30 per second activity in frontal, parietal and temporal areas. (LF) left frontal; (LM) left parietal, (LO) left occipital, (LT) left temporal, (R) similar areas on right side. (All EEGs were made on the Grass 6-channel electroencephalograph, using the "standard ground pick-up" with the ear leads as the "indifferent" electrodes.)

was an excellent 10–10½ per second but there was much 25–30 per second activity, most marked in the frontal, parietal and temporal leads plus frequent bursts of high-voltage 6–8 per second activity in all leads, with numerous positive spikes. There was no evidence of any focal pathology. There was a moderate "build-up" with overventilation, as noted by the appearance of large high-voltage 2–4 per second waves within 1½ minutes after the onset of overbreathing. These persisted for 20 seconds following three minutes of this procedure.

Frequent electroencephalograms were taken immediately following ligation of the left common carotid artery on 15 October 1943 (Fig. 3A, B, C, D,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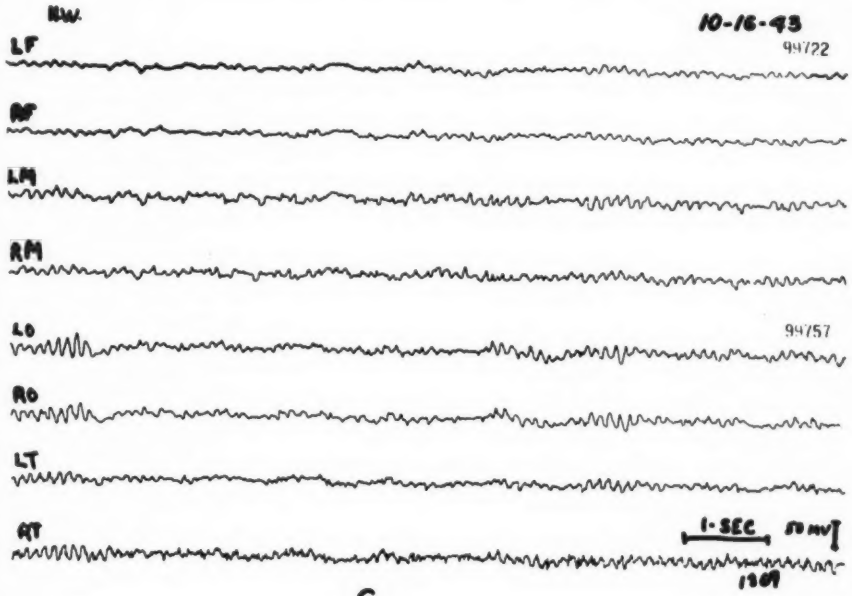
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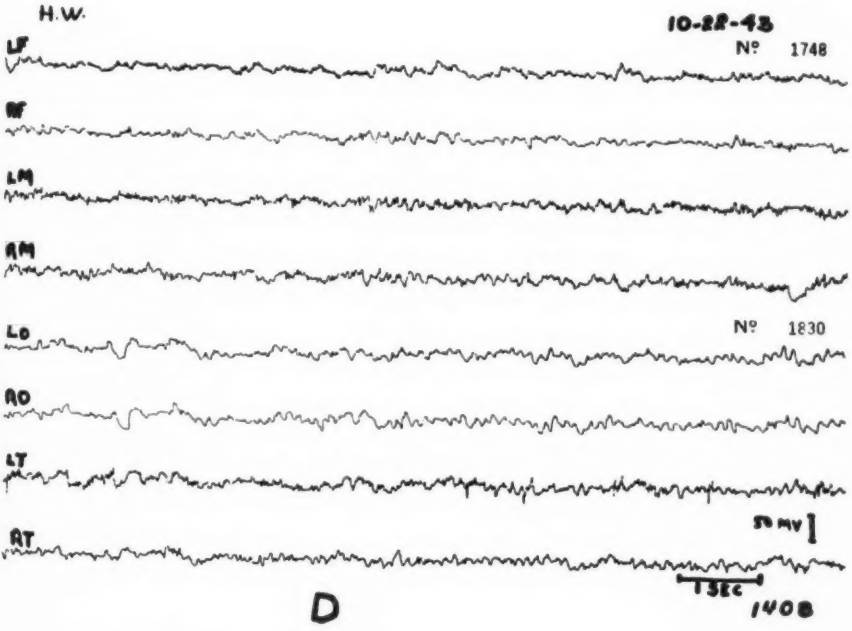
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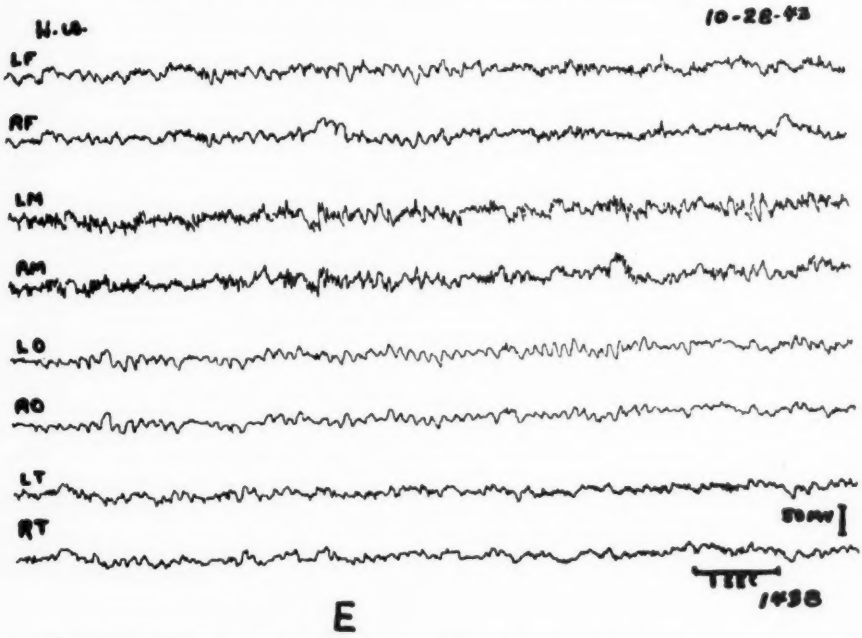
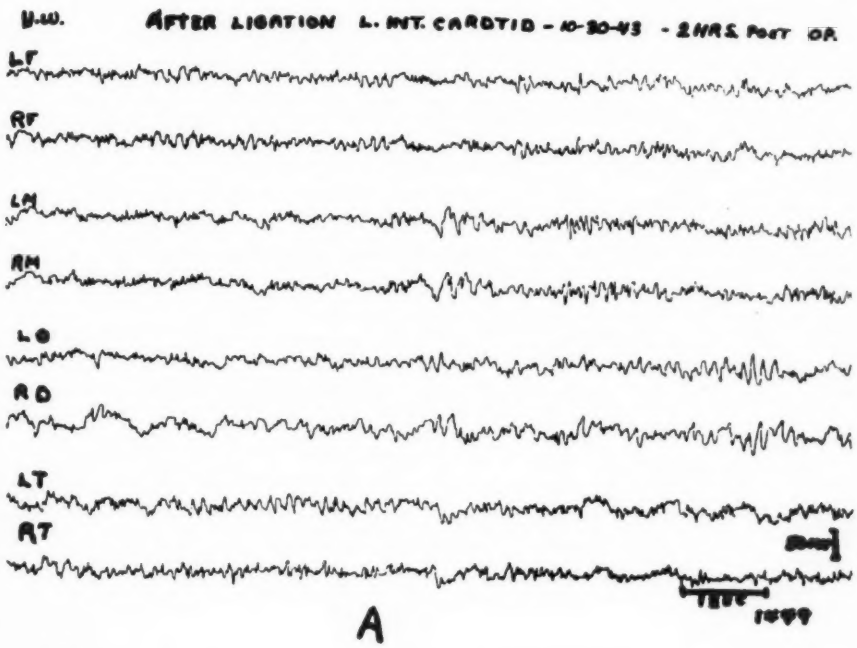


FIG. 3. EEGs following ligation of left common carotid artery 15 October 1943. Note: Generalized decrease in amplitude 1½ hours after ligation (A); increase in amplitude 4½ hours postoperatively (B); normal EEG on 16 October (C); recurrence of fast activity on 22 October synchronous with reappearance of subjective buzzing (D); more marked high-voltage fast activity on 28 October (E).

E). The record taken 1½ hours after ligation (when the buzzing had disappeared) showed only a generalized decrease in amplitude. Four and one-half hours postoperatively, although the generalized decrease in amplitude still persisted, the fast activity noted in the control electroencephalogram seemed to be decreasing in quantity and in amplitude. By 16 October 1943 (Fig. 3C) the dominant rhythm was an excellent 9 per second and no appreciable fast activity was seen. On 22 October 1943 a low-voltage fast activity of 18–25 per second began to reappear (Fig. 3D) and it is of interest that it was on this date that the patient noted the recurrence of the buzzing in his left ear. This high-voltage fast activity became more marked in subsequent days (Fig. 3E).

Two hours after ligation of the left internal carotid artery on 30 October 1943 the record showed predominantly high-voltage fast activity, again most marked anteriorly (Fig. 4A). Some 8 per second activity was seen in the occipitals. In both parietal regions a rare burst of high-voltage 3 per second waves was noted. There was no evidence of any focal discharges, although at this time a right Babinski was present. Five hours postoperatively the EEG showed much 14 per second activity, with frequent single discharges of high-voltage 3 per second waves without any focal discharges,


H.W.
AFTER LIGATION L. INT. CAROTID - 10-30-43 - 2 HRS. POST OP.
LF
RF
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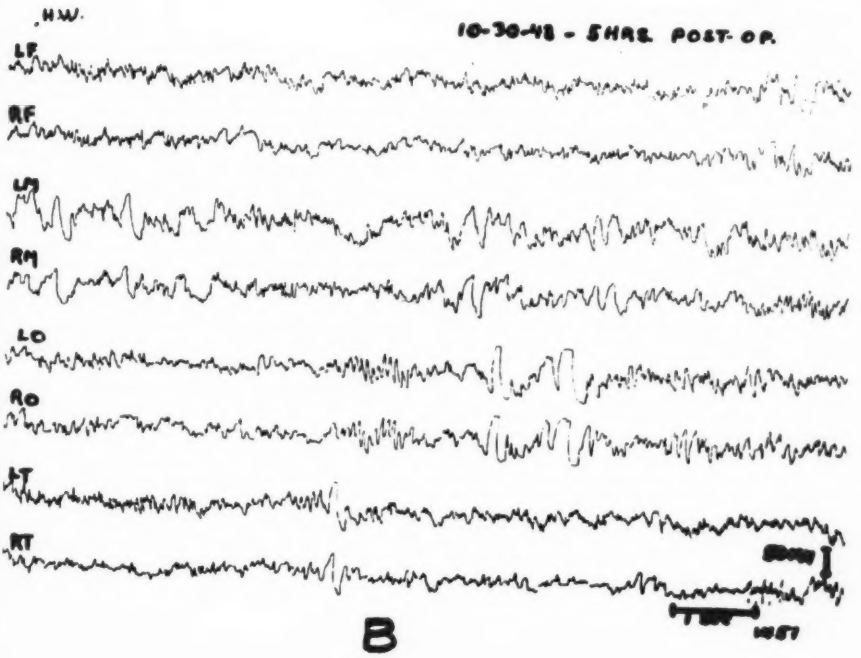
A


H.W.
10-30-43 - 5 HRS. POST-OP.
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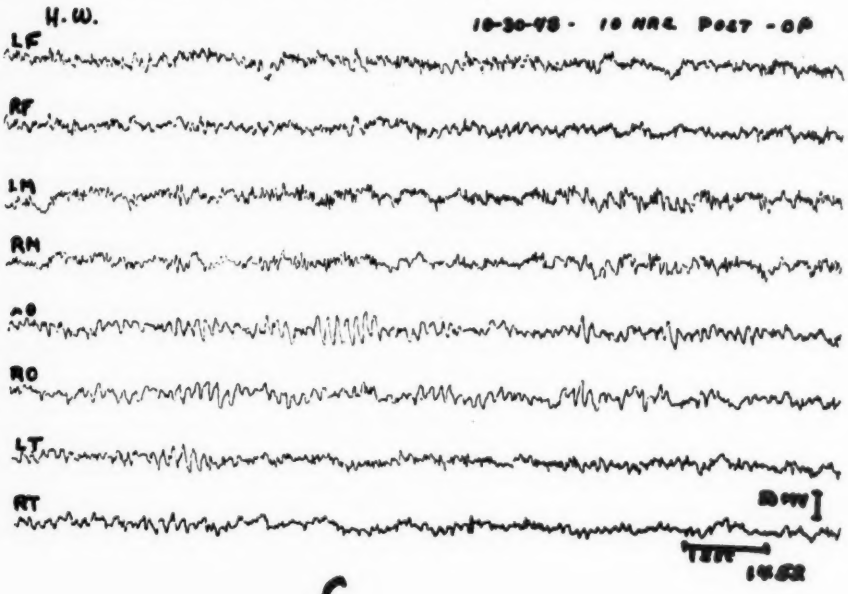
H.W.
10-30-43 - 10 MIN. POST - OP
LF
RF
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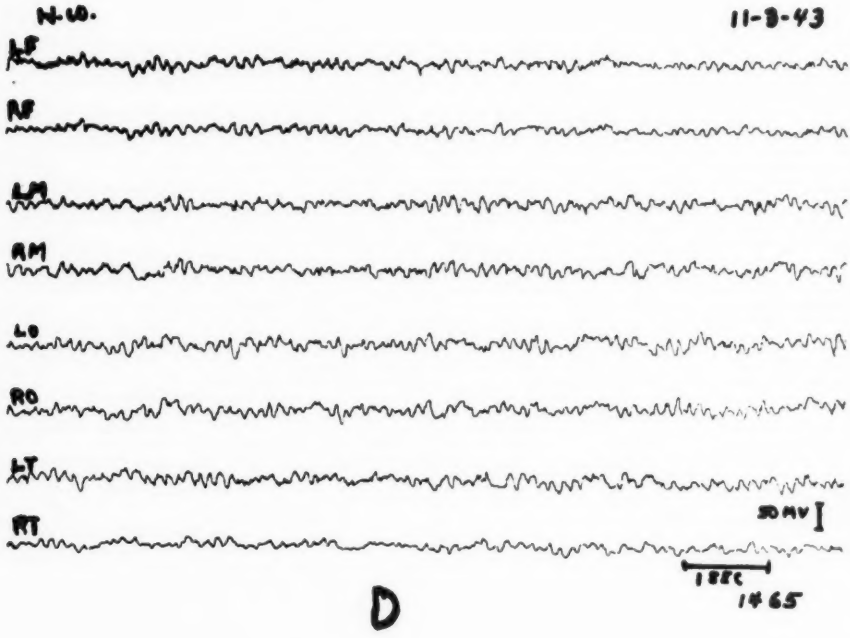
1462

C


N.W.
11-3-43
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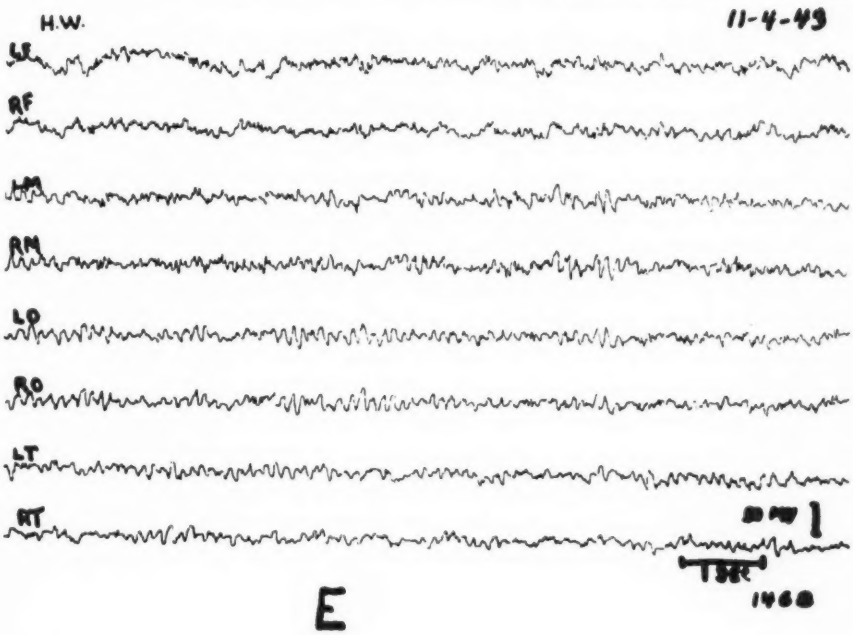
1465

D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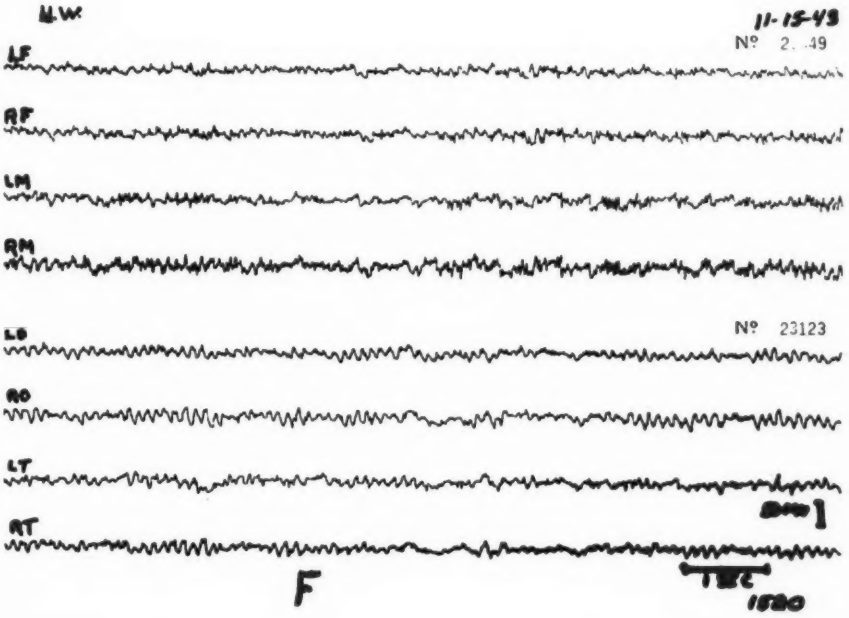
1460

E


H.W.
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1580

F

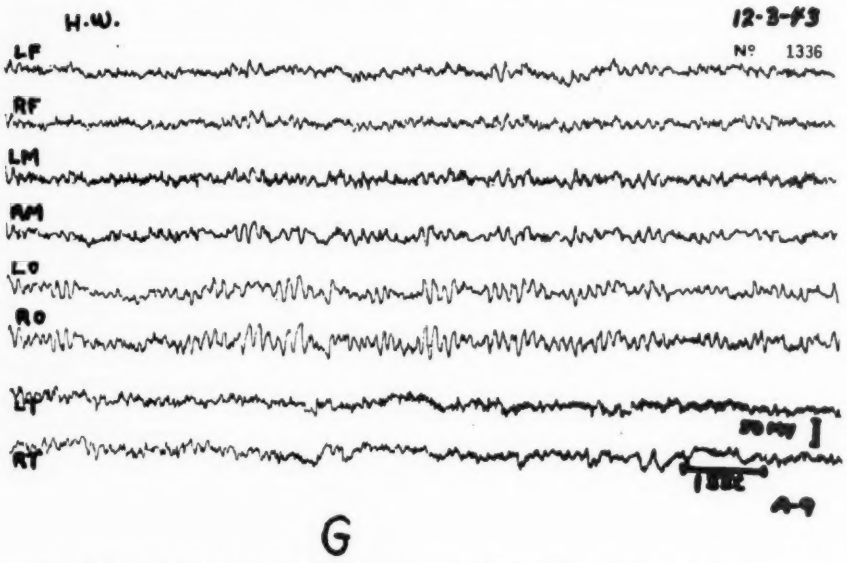
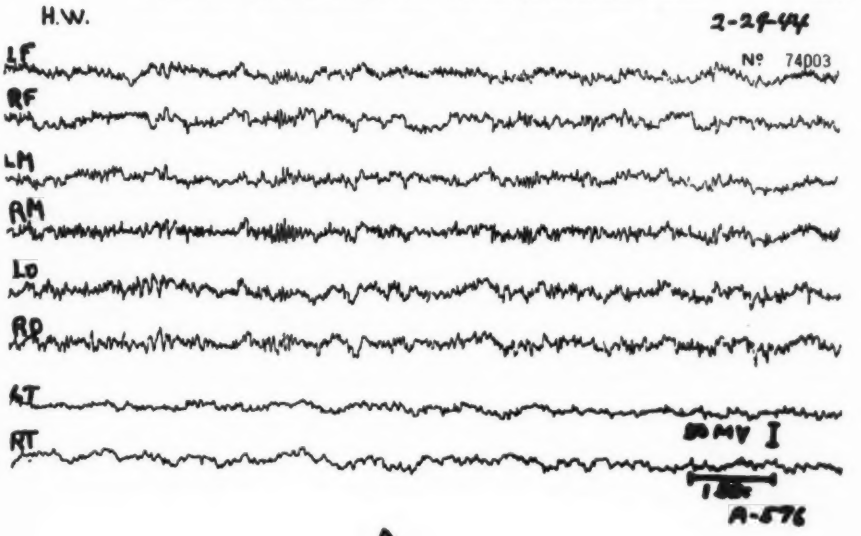


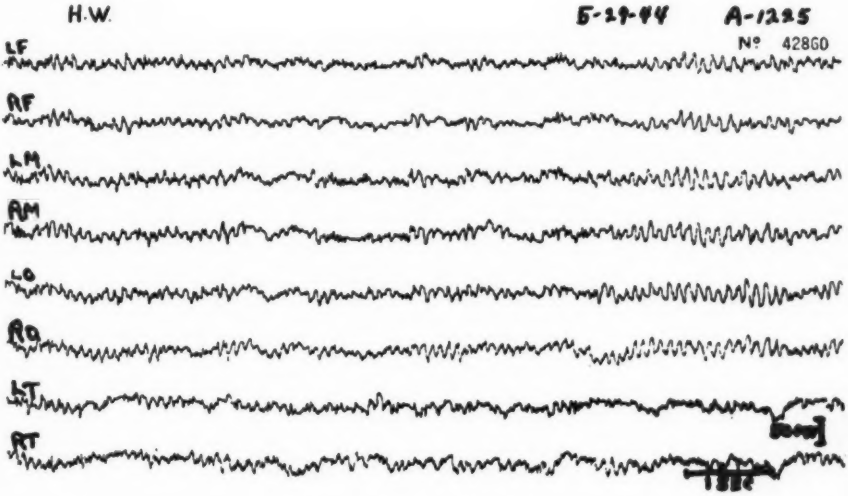
FIG. 4. EEGs following ligation of left internal carotid artery, 30 October 1943. Note: Rare bursts of 3 per second activity two hours postoperatively (A); frequent discharges of slower waves five hours postoperatively (B); disappearance of slow waves and recurrence of fast activity (C), 10 hours after ligation; variation in appearance of fast activity, usually synchronous with subjective buzzing (D, E, F, G).

and in spite of the fact that the patient was conscious and wide awake (Fig. 4B). Ten hours postoperatively the dominant rhythm was a good $8\frac{1}{2}$ per second in the occipital regions and there was much 25–30 per second activity in both frontal and parietal regions (Fig. 4C). The 3 per second waves had disappeared. By 3 November the fast activity had again completely disappeared and the dominant rhythm was now a good 8–$8\frac{1}{2}$ per second (Fig. 4D).

On 4 November the patient had begun to complain of an intermittent buzzing sensation in his *right* ear and it is of interest that whenever the buzzing was present the fast activity reappeared in the electroencephalogram (Fig. 4E, F, G and Fig. 5). By 13 December 1943 the buzzing was still intermittently present, but less marked, and it was noted that the fast activity appeared only after overventilation. The "build-up" with overventilation was now quite marked. From 15 December 1943 to the time of the block excision of the carotid bifurcation on 28 February 1944, the buzzing had completely disappeared and the fast activity in the electroencephalogram was only slightly in evidence in both frontal and parietal regions, if at all. Following operation on 28 February 1944 and subsequently, the buzzing in the right ear was intermittently present again, and usually corresponding to the time in which the buzzing was present fast activity was noted. The more intense the buzzing sound, the higher the voltage of fast activity (Fig. 5A, B).



A



B

FIG. 5. EEGs following block excision of carotid bifurcation. Note variation in appearance of fast activity in anterior electrodes, occurring simultaneously with the presence of subjective buzzing sound in *right* ear (A, B).

COMBINED ELECTROENCEPHALOGRAPHIC AND ELECTROCARDIOGRAPHIC STUDIES MADE WHILE MASSAGING EITHER CAROTID SINUS

Although between 1 October 1943 and 15 December 1943 numerous combined electroencephalographic and electrocardiographic studies were made while alternately massaging either carotid sinus with the patient in a recumbent posture, no evidence of a sensitive carotid sinus of either a central, cardiac or depressor type was noted. On 25 January 1944, following the onset

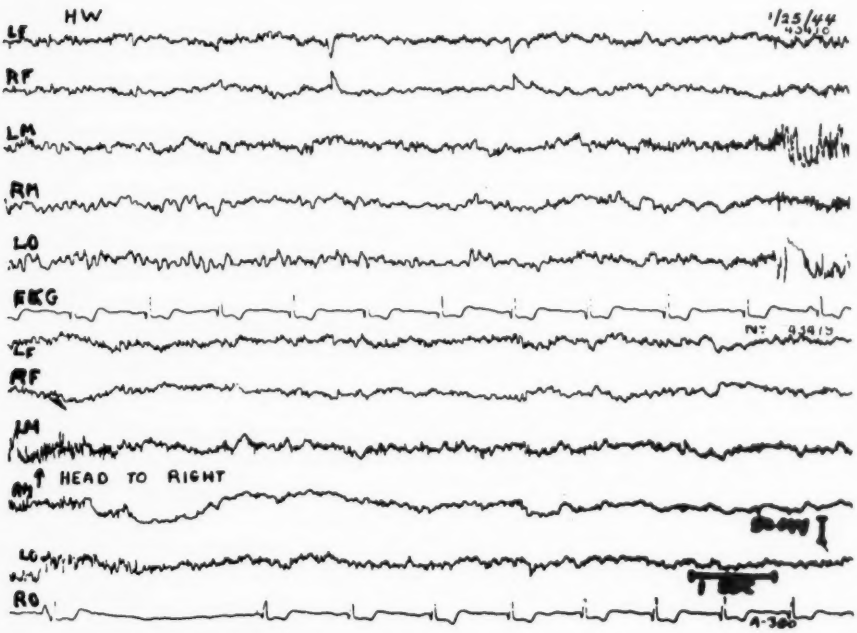
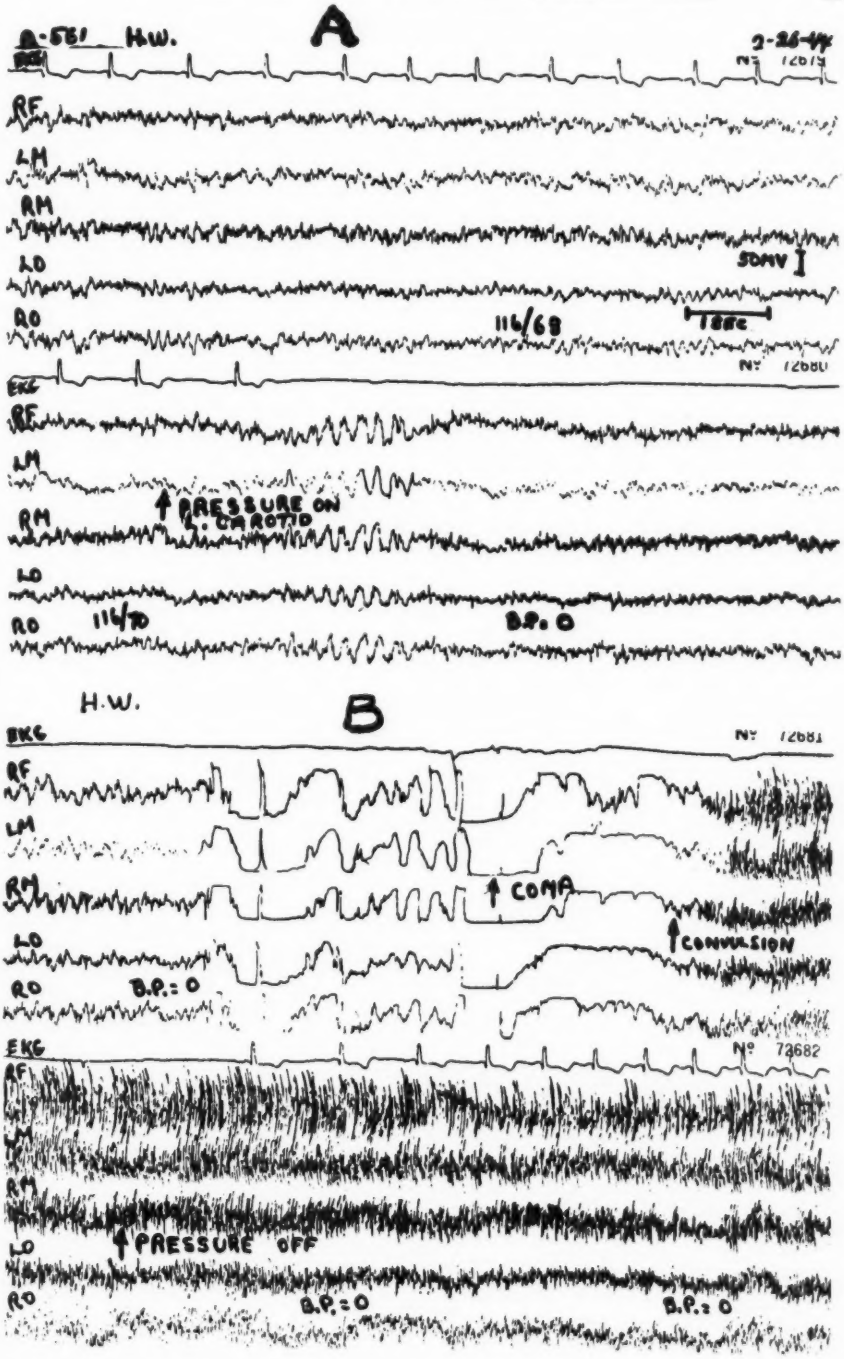


FIG. 6. Simultaneous EEG and EKG taken while patient turned head to right (see arrow). Note skipped beat in EKG. (Each strip represents a 10-second period; they run consecutively and continuously from right to left.)

of syncope, this procedure was repeated. As a control study the patient was asked to quickly turn his head to the right. Immediately following this there were one or two skipped beats, but no essential change in the electroencephalogram (Fig. 6). The left carotid sinus was then massaged. Within one second, a period of asystole lasting 20 seconds occurred (Fig. 7A, B). Two seconds after onset of massage, large high-voltage 3–4 per second waves appeared in the electroencephalogram, lasting about two seconds. At the same time the blood pressure fell to zero and coma supervened with the appearance of larger and slower EEG waves. Fourteen seconds after onset of massage, the patient had a right-sided convulsion which lasted 22 seconds (Fig. 7B, C). Following cessation of massage and pressure on the left carotid


A
H.W.
2-26-47
EKG
RF
LM
RM
LD
RO
116/68
1 SEC
PRESSURE ON L. CAROTID
116/70
B.P. 0
B
H.W.
EKG
RF
LM
RM
LD
RO
COMA
CONVULSION
B.P.: 0
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LD
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PRESSURE OFF
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B.P.: 0

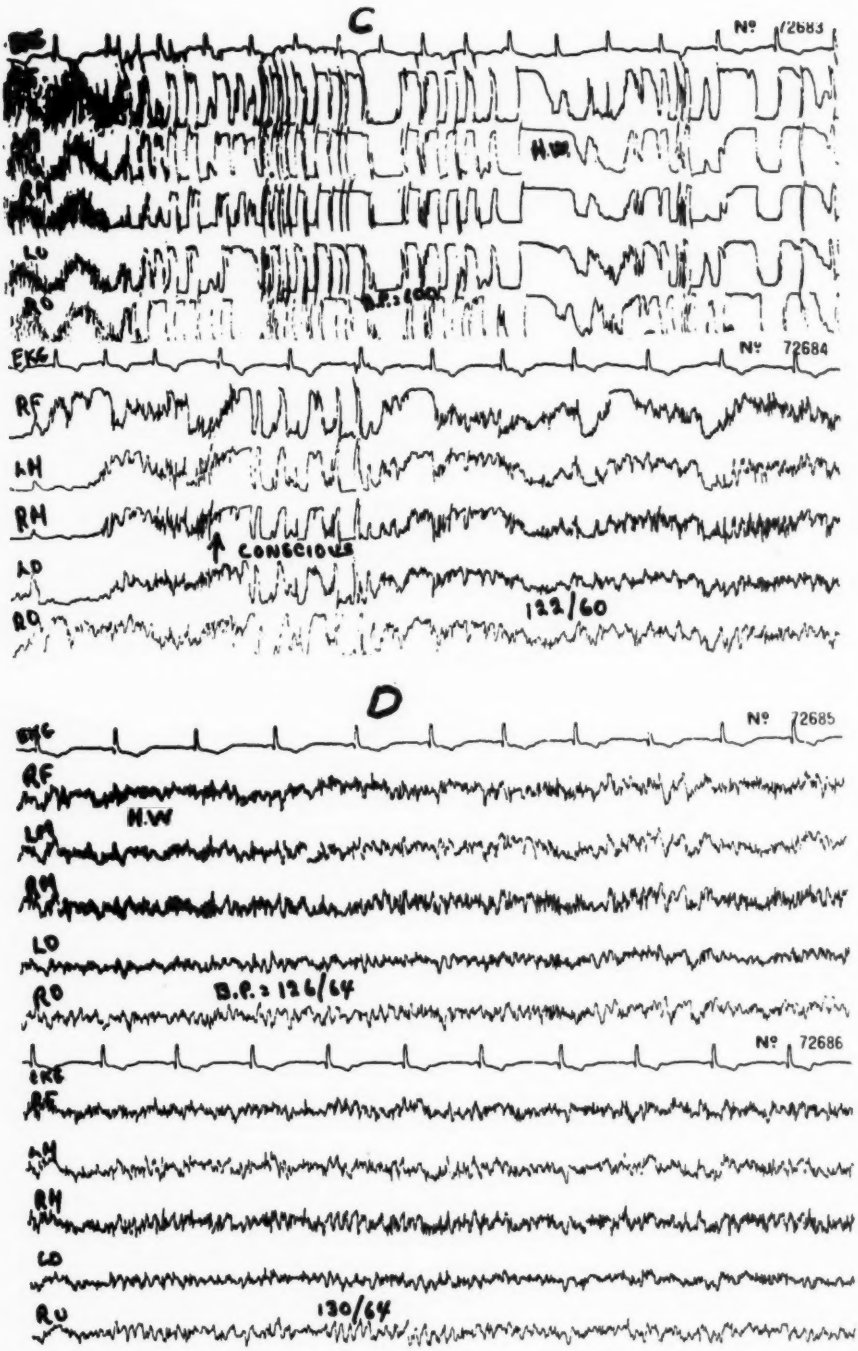
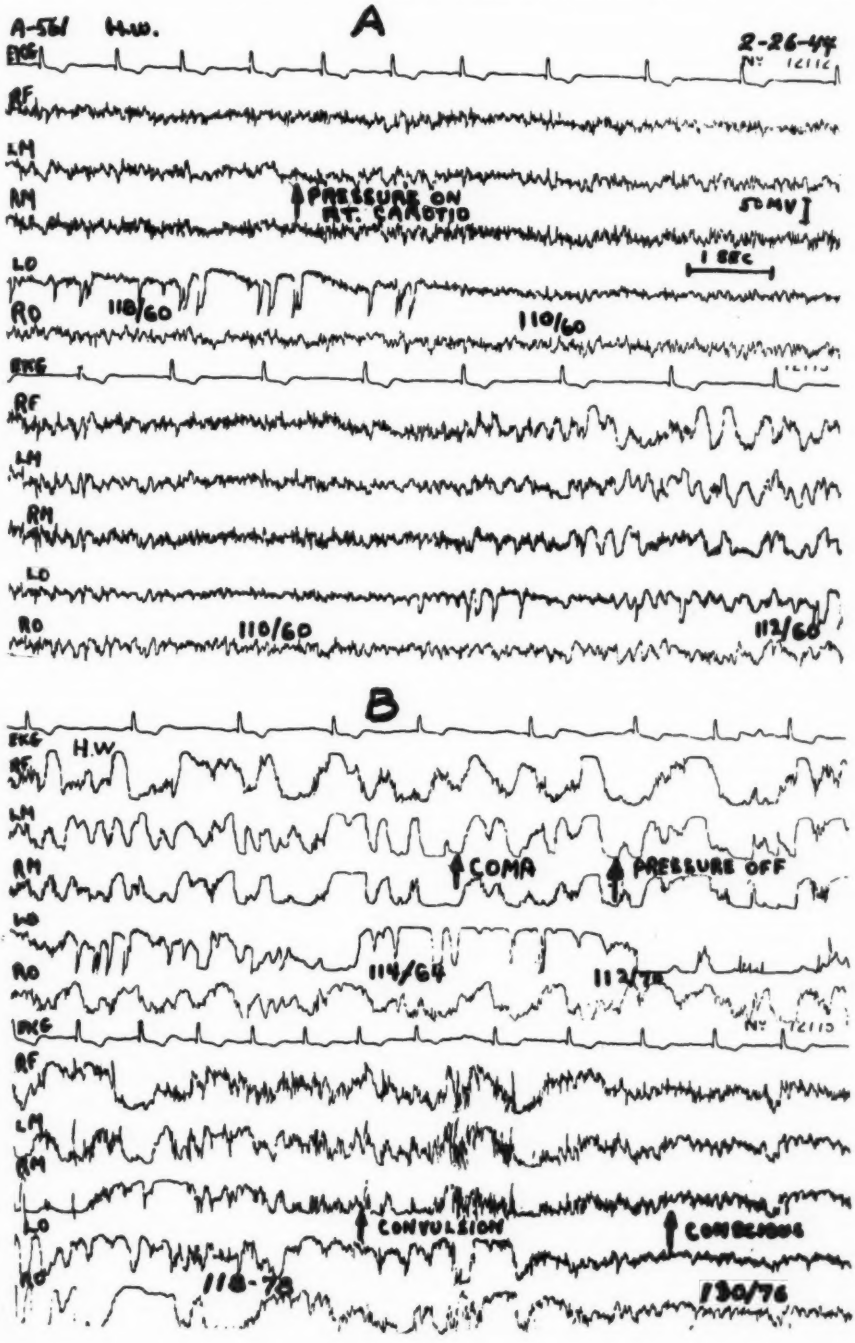


FIG. 7. Simultaneous EEG, EKG and blood pressure recordings while massaging and compressing the left carotid sinus. Note: Onset of asystole one second after onset of massage, lasting 20 seconds (A, B); appearance of high-voltage 3–4 per second waves in EEG within two seconds (A), fall of blood pressure to zero (A), followed by coma and convulsion (B); return to resting state after cessation of massage (C, D). (Each strip represents a 10-second period; they run consecutively and continuously from right to left.)


A
A-561 H.W.
2-26-47
EKG
RF
LM
RM
PRESSURE ON RT. CAROTID
5 MV
1 SEC
LD
RD
110/60
110/60
110/60
112/60
B
EKG
H.W.
RF
LM
RM
COMA
PRESSURE OFF
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112/78
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CONVULSION
CONSCIOUS
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118-78
130/76

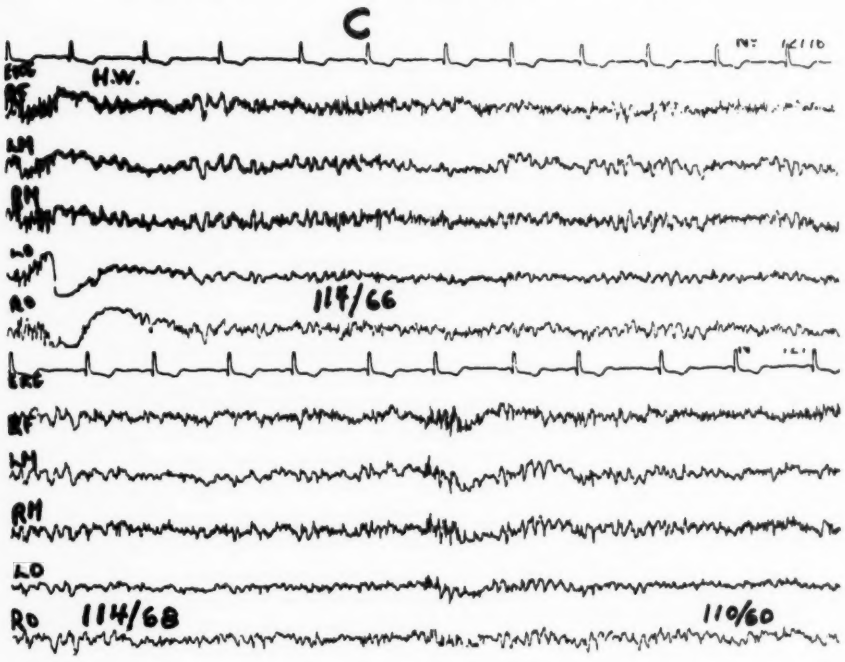

FIG. 8. Simultaneous EEG, EKG and blood pressure recordings while compressing the right carotid sinus region. Note: Relatively slight slowing in pulse rate and no change in blood pressure (A, B); appearance of high-voltage slow waves in EEG within 13 seconds after compression (A, B), followed by coma and convulsion (B); rapid return to normal state after release of pressure (C).

sinus, the electroencephalogram, electrocardiogram, and the blood pressure rapidly returned to normal (Fig. 7C, D).

As a corollary a similar procedure was carried out while compressing the right carotid sinus region (Fig. 8). There was relatively little slowing in the pulse rate and no notable change in the blood pressure. However, within 13 seconds following the onset of pressure, large slow waves appeared (Fig. 8A) followed by coma and left-sided convulsion (Fig. 8B), with a rapid return to the normal state after release of pressure (Fig. 8B, C). This phenomenon was apparently due to cerebral ischemia from compression of the remaining carotid vessels.

Following excision of the left carotid body (Fig. 1) on 28 February 1944 this procedure was repeated on numerous occasions until 1 August 1944, with no essential change in the EEG, EKG, blood pressure or in clinical responses. Thus, the sensitive carotid sinus had been completely excised. Responses similar to those previously noted were always evinced on the right side.

SUMMARY

An unusual case of a sensitive carotid sinus syncope developing after ligation of the common carotid and internal carotid arteries is presented. The patient originally had multiple severe injuries about the head, with the resultant production of an arterio-venous aneurysm of the left internal carotid artery and cavernous sinus. An unusual opportunity for follow-up was afforded by the use of the electroencephalogram and the electrocardiogram. The control electroencephalogram was marked by the presence of high-voltage fast activity which disappeared with the abeyance of the subjective noises in the head and reappeared with the intermittent presence of the swishing sounds heard by the patient. The sensitive carotid sinus appeared on the side of the ligated carotid vessels some two months after operation and is attributed to scar-tissue formation, with resultant tension stimulation of the left carotid sinus each time the head was turned to the right. Electroencephalographic and electrocardiographic tracings of the syndrome are recorded. Cure of the sensitive left carotid sinus occurred following complete excision of the carotid bifurcation.

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HISTOLOGIC STUDIES OF THE BRAIN FOLLOWING HEAD TRAUMA

I. POST-TRAUMATIC CEREBRAL SWELLING AND EDEMA

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THE TERMS cerebral concussion, edema, and contusion are familiar to both the clinician and the pathologist. Often, however, the words have different connotations for them, and until relatively stable definitions are established, confusion will persist. It is our purpose to review in several papers some of the changes associated with injury to various parts of the central nervous system in an effort to clarify terms and to correlate more closely clinical and pathologic findings, in the hope that thereby a broader basis may be laid for therapy.

In these papers we propose to stress the occurrence of vascular alterations, and to interpret their effects on nervous tissue, because we believe that exploitation of this rather neglected line of approach is promising, even though it may well prove but a partial answer to the problem of nervous system trauma.

We define as cerebral concussion that state of altered consciousness that occurs in association with sudden acceleration or deceleration of the brain,[1] and we regard it as a disturbed physiologic state for which there can be found with our present methods no definite anatomical substratum or, at most, minimum cellular alterations.[8] However, it seems likely that altered activity in the brain stem reflexes with resultant respiratory, blood pressure, and vasomotor changes may contribute to the circulatory disturbances to be discussed in this and subsequent papers.[3,4,5,6]

In the literature dealing with the clinical aspect of "head injury," frequent reference is made to the occurrence of cerebral edema. The term appears to be employed to designate a clinical state that is thought to be due to an increase in tissue fluids within the brain. The correlation between the clinical and the pathologic condition is still indefinite, and as indicated by Pilcher,[9] and by White and his co-workers,[14] much information is needed in order to arrive at a satisfactory explanation of the morbid physiology.

It is our belief that the condition referred to loosely by clinicians as cerebral edema is represented pathologically by two states, one of which merges rather insensibly into the other, edema and its precursor, brain swelling.

Macroscopically in the fixed brain, there is rather little to differentiate the two conditions, which are characterized by an increase in brain volume, some convolutional flattening, and by increased volume of the white substance which results in narrowing and compression of the gray matter. In addition the ventricles are apt to be compressed, and, in unilateral swelling or edema, to be shifted.

The differentiation between the two conditions is made histologically, and the criteria of recognition, as already specified by one of us in cases of brain tumor,[10,11,12,13] have been found in this study to apply in instances of brain injury also. There are in edema the alveolar and sieve-like appearance of the nervous tissue and distention of the perivascular and pericellular spaces, the resultant liquefaction of nervous tissue, amoeboid degeneration of the astrocytes, and significantly, in the more advanced stages, signs of vascular stasis: congestion and engorgement of the capillaries and veins, perivascular accumulations of fluid and even of cellular elements, and occasionally evidence of endothelial necrosis.

In post-traumatic brain swelling the changes are of lesser degree. The parenchymal changes are less striking and consist chiefly of hydration and swelling of the axis cylinders, myelin sheaths, and glial cells. These changes, particularly those of the nerve fiber and medullary sheath, are easily overlooked in hematoxylin and eosin preparations, but are evident on careful study of silver impregnations, such as the Bodian, or with the Loyez stain.

The present report is based on a review of the accumulated material of seven years from a large and active "head injury" service, and an intensive study of the material derived in the past three years.

A typical instance of each condition, swelling and edema, will be cited.

A. BRAIN SWELLING

Case 1. *Severe head injury three years previously. Recent acute head injury. Early development of extradural clot. Evacuation of clot: operative death. Necropsy: histologic changes indicative of cerebral swelling.*

D.G., a 30-year-old bartender and chronic alcoholic, had suffered a severe head injury three years previously, when a sharp object was driven into the skull over the left eye. He was unconscious for a few hours, was hospitalized for about two months, and then apparently made an uneventful recovery.

On the night before his final admission he was assaulted and fell striking the back of his head resoundingly on the pavement. He was unconscious for a few minutes, but thereafter walked home, where he was found unconscious the following morning. On admission to the hospital he was thought to be intoxicated. That evening he was seen by a neurologic consultant. Examination showed him to be stuporous. He responded to painful stimuli by vigorous movement of the right arm and leg. The optic discs were not remarkable, the pupils were fixed bilaterally at 4 mm., and there were a left facial paresis, weakness of the left extremities with increased tone, hyperreflexia, and a positive Babinski response on the left side. There were strong and purposeful movements of the right arm and right leg; the right plantar response was also extensor.

Lumbar puncture showed a pressure of 200 mm. of water; the fluid contained 24,000 red blood cells per c.mm. Roentgenograms of the skull revealed no fracture.

He was taken to the operating room and a right subtemporal opening was made. There was a transverse fracture line running across the temporal bone and an extradural clot, 4 cm. in depth at its greatest thickness, extended from the frontal to the occipital region. This was evacuated, but the brain showed no tendency to fill out. Respirations ceased before the operation was terminated, the pulse became rapid and thready, and the blood pressure fell. Death occurred on the operating table approximately 28 to 30 hours following his injury.

Necropsy. The residuals of an extradural clot, measuring 10 cm. in diameter, were present over the occipito-parietal region. The underlying brain was flattened. Inspection of the median cleft revealed a displacement of the cingulate gyrus under the free edge of the falx.

The undersurfaces of the frontal lobes showed signs of the old injury, with considerable loss of substance and replacement gliosis, which were more evident on the left. As a manifestation of the recent injury there was a well defined herniation of the uncal portion of the right temporal lobe, measuring 2.5 cm. in length and 1.3 cm. in width. The pons and optic chiasm were shifted to the left by the herniation.

Coronal sections (Figs. 1 and 2) showed definite increase in bulk of the right hemisphere, more evident in the white matter than in the gray. There was a shift of the ventricular system

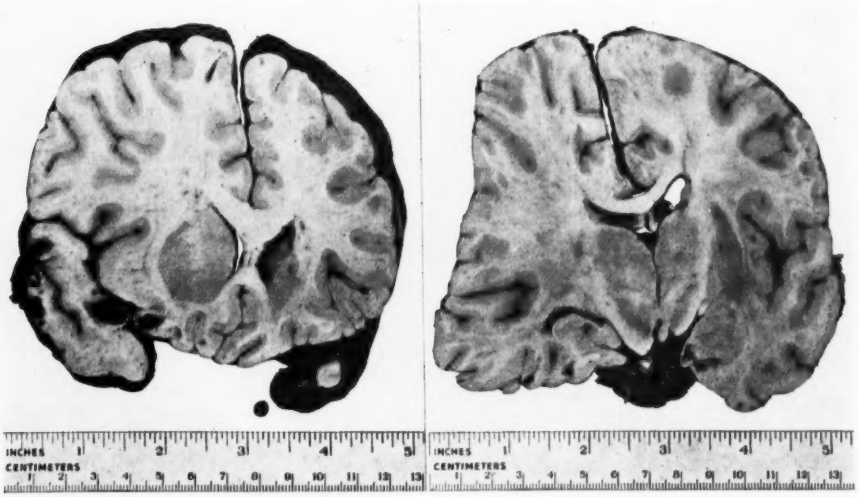

FIG. 1 (*left*). Case 1. Swelling of the right hemisphere with enlargement of the white matter. Note shift of the midline structures to the left and compression of the right lateral ventricle. The cut appears to be asymmetrical; actually the cut is true but the posteriorly placed clot has shifted the anterior portion of the right hemisphere forward.

FIG. 2 (*right*). Case 1. Increase in bulk of the right hemisphere associated with a transtentorial herniation of the right hypothalamic region. Note downward displacement of the right substantia nigra and peduncle and indentation of the right, and in a lesser degree of the left, uncus by the free edge of the tentorium. The herniated uncus on both sides shows scattered areas of petechial hemorrhages. The symmetry of the cut makes the reality of the swelling more evident than does Fig. 1.

to the left. The right basal ganglia appeared swollen, and the right lateral ventricle was compressed.

In association with the uncal herniation on the right there was a displacement of the right hypothalamic region downward and mesially into the incisural notch (Fig. 2). There was also displacement of the substantia nigra and of the peduncle of this side. A few scattered hemorrhages were to be seen at the level of the inferior colliculi and the gray matter of the tegmen. In addition there were scattered petechial hemorrhages in the lower lip of the Sylvian fissure on the right and in the right temporal lobe, particularly in the herniated portion of the right uncus. The white matter of the right hemisphere showed a moderate degree of congestion with occasional perivascular extravasations of lymphocytes.

The cerebellum and medulla appeared grossly normal. The blood vessels at the base were normally distributed and were of normal appearance.

Microscopic Observations. Survey sections from the white and gray substance of both hemispheres, from the hypothalamus, and the midbrain were stained with hematoxylin and eosin and with cresyl violet, and were also prepared by the Loyez and Bodian methods.

The white matter of the right hemisphere showed swelling of all the constituent elements, both parenchymal and interstitial. These changes were not evident in the hematoxylin and eosin preparations, but careful analysis of the Bodian and Loyez sections disclosed findings ranging from hydropic swelling of the axis cylinders and the myelin sheaths to more severe alterations indicated by ragged outlines and signs of gradual disintegration of the nerve fibers. The myelin sheaths disclosed irregularities in contour with many large globules and granules of lipoid. The axis cylinders showed not only diffuse swelling, but many small fusiform varicosities, throughout their course and at their termination (Fig. 3).

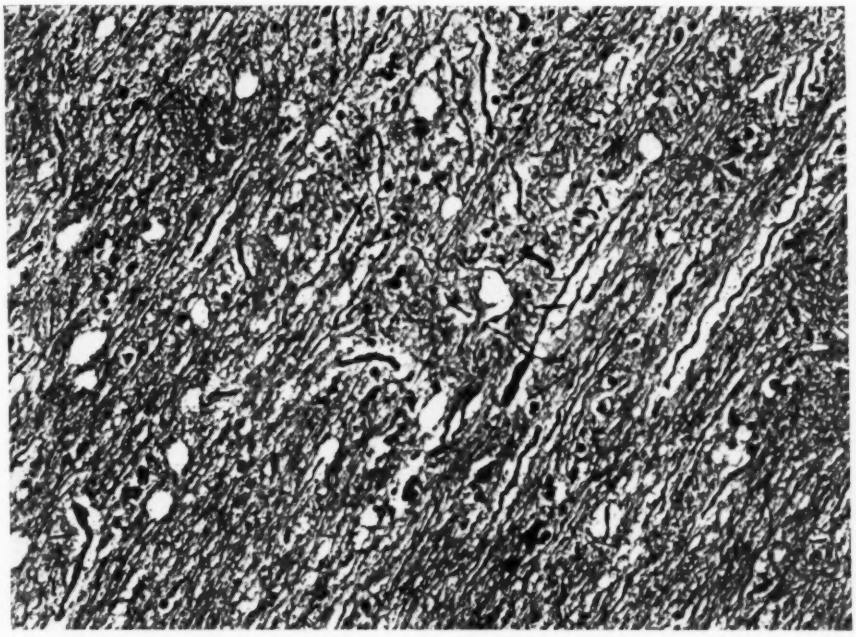

FIG. 3. Case 1. Diffuse swelling of the nerve fibers associated with formation of small fusiform varicosities throughout their course and at their fragmented ends. Bodian silver impregnation, ×220.

In all of the sections from the right hemisphere there was rarefaction of the tissue indicated by a loose reticular appearance, which was most evident in the white matter of the centrum semiovale and which was less intense near the cortex. The subcortical U fibers were comparatively well preserved.

Glial changes consisted chiefly in hydropic swelling of the oligodendroglia, occasionally by evidence of disintegration of the cell bodies. There were also associated clasmatodendrosis and occasional amoeboid degeneration of the astrocytes.

No definite vascular abnormalities were detected except for a moderate degree of dilatation of the smaller blood vessels and occasional distention of the perivascular spaces, which were sometimes filled with transuded serous fluid. Here and there were present areas of perivascular hemorrhage and in these zones the typical signs of vasoparalysis could be found.

The cortical ribbon appeared normal.

B. CEREBRAL EDEMA

Case 2. *Severe head injury due to repeated blows with a blunt instrument. Transient loss of consciousness followed by victim's own search for help; subsequent coma. Absence of focal signs; high lumbar puncture pressure. Death forty-eight hours after injury. Necropsy: histologic changes indicative of cerebral edema.*

R.R., a white male of 53, was admitted to the hospital on January 20, 1939. Some twelve to eighteen hours earlier, he had been repeatedly beaten over the head with a shotgun and left for dead. Subsequently he regained consciousness and after some hours was brought to the hospital from a physician's office.

On admission he was deeply cyanotic and gasping for breath. The difficulty was promptly relieved by elevation of the chin and establishment of a proper airway (one can only speculate

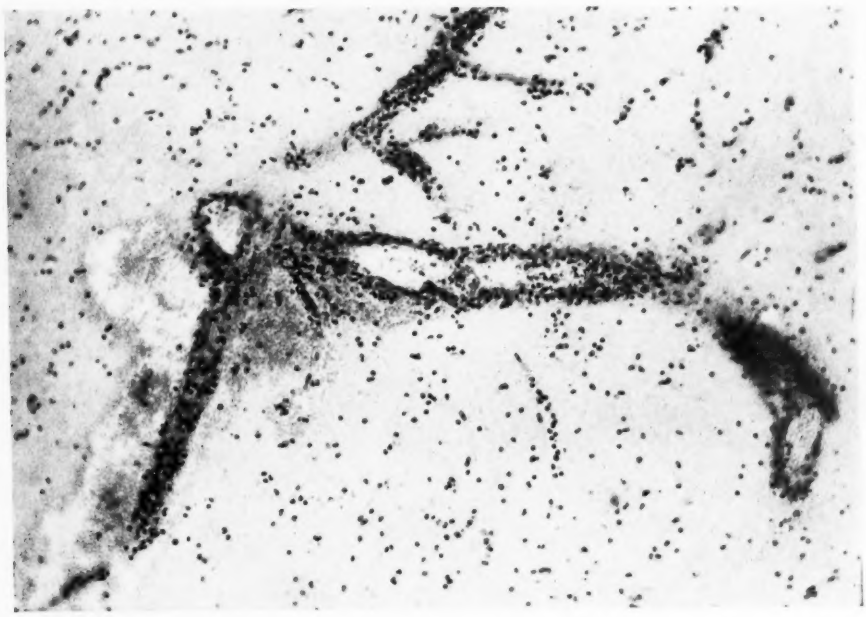

FIG. 4. Case 2. Advanced stage of vascular alteration characterized by distention of veins and capillaries associated with disintegration of their walls and increased permeability for serous fluid and red blood cells. ×140.

what the effect of the prolonged cyanosis may have been on the outcome of the case). Further examination showed him to be deeply comatose, flaccid, and unresponsive to painful stimuli. The temperature was 99, pulse 92, respirations 26, and the blood pressure 130/40.

The head displayed diffuse edema and four scattered lacerations, bilateral Battle's signs, a huge hematoma of the right eye with subconjunctival hemorrhage, and dried blood in the auditory canals, in the nose, and in the mouth. General examination was otherwise negative. Neurologic examination revealed no localizing signs.

Lumbar puncture on admission showed an initial pressure of 300 mm. of water; the fluid contained 350,000 red blood cells per c.mm. Skull films revealed a questionable fracture in the external orbital wall on the right, and another beneath the anterior clinoid processes. Shortly after admission the patient began to be very restless and continued so for the remaining 32

hours of his life, despite sedation. Lumbar puncture 40 to 48 hours after the assault and four hours prior to death showed an initial pressure of only 30 mm.; presumably the low pressure was due to relative dehydration, or possibly to cerebrospinal fluid block at the tentorium or foramen magnum. He was found dead in bed four hours after the lumbar puncture was performed.

Necropsy. In addition to a terminal bronchopneumonia, there were linear fractures of both temporo-parietal regions, and bilateral extradural hemorrhages, that on the left being insignificant, that on the right measuring 5 × 2 cm. in circumference and up to 1 cm. in thickness.

FIG. 5. Sieve-like appearance of the nervous tissue with distention of the pericellular and perivascular spaces which harbor large amounts of serous fluid. Note distention of the smaller veins and early stage of degeneration of their walls. The nerve cells show signs of ischemic degeneration. Hematoxylin and eosin, ×140.

There was a minimal subdural hemorrhage on the left overlying a superficially contused temporal lobe. There was diffuse subarachnoid hemorrhage.

Cross sections of the brain showed the ventricles to be of normal size and to be in normal position. Throughout the brain there was a very moderate vascular congestion, particularly in the white matter.

Microscopic Observations. Sections were taken from different parts of the centrum semiovale and from the cortical gray matter. Those of the white matter revealed both vascular changes and diffuse changes in the parenchyma. Fig. 4 illustrates an advanced degree of vascular alteration. Most of the vessels exhibited distention of their lumina and varying degrees of degeneration of the walls, associated with an increased permeability for serous fluid and, at times, for red blood cells. The perivascular spaces were tremendously distended with fluid.

The changes in the parenchyma consisted of reticular appearance of the tissue due to the distention of the pericellular and perivascular spaces (Fig. 5), and necrobiosis of the ganglion cells. Most of the neurones showed signs of ischemic degeneration: shrunken cytoplasm, dis-

appearance of the Nissl bodies, and darkly staining nuclei. Cells of this type were scattered diffusely. In some areas, almost every neurone was affected in this manner. The nerve fibers, separated by the accumulations of serous exudate in the interspaces, revealed no signs of destruction. Only a few of the axones were thickened and showed irregular varicosities and end bulbs. Myelin sheath preparations revealed a diffuse pallor and also irregular thickening and degeneration of a few of the myelin sheaths. Diffuse changes in the macroglia were observed, ranging from irregular increase in size of cell bodies and granular appearance of the cell processes to advanced changes typical of clasmatodendrosis. The meninges appeared distended.

COMMENT

Case 1 presents the histologic findings of a condition that we regard as the precursor of cerebral edema, namely cerebral swelling. Its existence is characterized by the histologic evidence of swelling of the nerve fibers, the myelin sheaths, and the glia, particularly the oligodendroglia. These changes are not evident in the usual hematoxylin and eosin preparations, but may be clearly identified in silver preparations where they are predominant in the central white matter.

In this stage the reaction presumably is a reversible one, but if the circumstances are unfavorable it appears to progress insensibly from a stage of increased intracellular fluid accumulation into that of cerebral edema, characterized microscopically by distention of the perivascular and pericellular spaces, transudation of serous fluid into the nervous tissue about the blood vessels with resultant liquefaction of the tissues, and the production of an alveolar and sieve-like appearance of the tissue. Amoeboid degeneration of astrocytes also occurs.

What is the origin and physiopathologic mechanism of post-traumatic swelling and edema?

We believe that the histologic changes described in and about the blood vessels in our cases provide the important clue to the mechanism. We consider both the increased amount of tissue fluid and the tissue changes to be secondary to local circulatory disturbances. On the basis of these observations, we suggest the following theory of the mechanism: As the result of trauma obvious superficial damage with cortical bruising and laceration may occur. But in addition there are alterations in the deeper structures of the brain which likewise demand explanation, particularly the often striking changes in the white matter.

We believe that there occurs transmission of the energy accompanying the traumatic insult to the deeper portions of the brain, and that the transmitted force causes vasoparalysis of the capillaries and venules of a degree sufficient to cause actual slowing of the blood stream. With the swelling of the tissue there presumably occurs an increased venous pressure, and it is even conceivable that there may occur actual reversal of the normal direction of fluid exchange. Local accumulation of carbon dioxide, because of less effective circulation, leads to further vascular dilatation and to increased permeability of the vessel wall. If these alterations be sufficiently severe, actual structural changes may occur in the capillaries and veins. The

developing edema of the tissue then serves in turn further to retard circulation and contribute to hypoxia, and no doubt these physiologic changes interfere with proper oxygen and carbon-dioxide exchange, so that the normal cycle becomes more and more disturbed and incompatible with the maintenance of local function. Should this local function be of vital importance, e.g., that of the respiration or of temperature control, and should the impairment of activity become sufficiently severe, death will result. Should, on the other hand, the changes occur in a non-vital region, loss of function, temporary or permanent, may result in a clinical deficit depending on the specific circumstances of site, severity, and duration of impairment.

Such an hypothesis need not suppose the activation of a neurovascular network, which has not yet been demonstrated except for the larger cerebral vessels. The experimental work of Echlin,[2] though limited to vasoconstriction produced in the pial arteries of animals by electrical and mechanical stimulation, confirms and amplifies the work of other authors, including Florey.[7] That similar mechanical changes may occur in the deeper vessels supplying both the gray and the white matter seems not too gross an assumption for our working hypothesis.

From the clinical point of view one must accept the reality of cerebral swelling and edema. Their recognition in the patient may actually be difficult and the differentiation from other post-traumatic states associated with increased intracranial pressure may present a problem. From this limited clinico-pathologic study, nothing positive can be said concerning clinical recognition.

SUMMARY

1. Post-traumatic brain swelling and cerebral edema are described in detail clinically and histologically.

2. The histologic changes described as accompanying cerebral edema are interpreted in terms of functional vascular disturbance. Cerebral swelling is believed to be a precursor of edema and the mechanism responsible for its occurrence is regarded as the same, but of lesser degree.

3. The changes characterizing edema consist in pericellular and perivascular accumulations of fluid, but there are to be emphasized the signs of functional vascular disturbance: congestion, stasis, dilatation of capillaries and veins, and occasional evidence of endothelial necrosis.

4. The changes characterizing brain swelling consist chiefly of swelling of the axis cylinders, myelin sheaths, and glial cells. These changes are poorly shown in routine stains, but are evident in the silver impregnations.

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THE HOMOLOGOUS AND HETEROLOGOUS TRANSPLANTATION OF BRAIN AND BRAIN TUMORS*

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SEVERAL years ago it was shown that human and other mammalian cancers could be readily transferred to animals of alien species by utilizing the anterior chamber of the eye as a transplantation site.[3] Subsequent investigations undertaken to determine the limits of heterotransplantability demonstrated that the capacity to grow in a foreign host was shared by embryonic tissue but was not a property of normal adult tissue, benign tumors or potentially malignant tumors in preinvasive stages,[1,2] Tissues of the nervous system were included in these experiments and the results obtained seemed of sufficient interest and promise from a neurological viewpoint to warrant separate presentation.

The present paper will be limited to a report of transplantation experiments utilizing brain and meninges; a second paper will be concerned with similar investigations involving peripheral nerves. It should be emphasized from the beginning that the work to be described represents only a cursory examination of nervous tissues with respect to transplantability and that the primary object of these papers is to indicate a method of investigation rather than to report a detailed morphological study.

MATERIALS AND METHODS

The experiments to be described were concerned with an investigation of the transplantability of adult, embryonic and neoplastic brain tissues including the meninges in homologous and heterologous species.

The adult and embryonic tissues used in the study were obtained from human, rabbit and guinea pig sources. The neoplastic tissues consisted of an experimentally induced mouse glioma and a number of human tumors, including 5 meningiomas and 3 glioblastoma multiforme. The human tumors and adult brain tissue were biopsy specimens, while the embryonic brain tissue was derived from embryos delivered for therapeutic reasons between the second and third months of gestation. Rabbit and guinea pig embryonic brain tissue was obtained at different stages of gestation from the 7th to the 30th day. The mouse brain tumor was induced with methylcholanthrene according to the method described by Zimmerman and Arnold.[5] Guinea pigs were used as alien hosts for human tissues throughout the experiments. The heterologous transfer of rabbit and guinea pig tissues was accompanied

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in all instances by coincident transfer of fragments of the specimen to animals of the same species. Homologous control experiments of this nature obviously could not be carried out in the case of human material.

The anterior chamber of the eye was used as a transplantation site. The technique of transfer is extremely simple. After local anesthesia, the anterior chamber is opened close to the corneo-scleral junction by a short quick jab with a double-edged corneal knife. A small amount of fluid is allowed to escape and a fragment of tissue measuring less than a millimeter in diameter is inserted by means of a trocar. The corneal incision is not closed and, in order to avoid the possibility of escape, the fragment is forced into the inferior angle of the iris by applying light pressure along the corneal surface with a blunt instrument.

RESULTS

The present study was undertaken primarily to determine the transplantability of central nervous tissues together with their membranes and

TABLE I

Results of the homologous and heterologous transplantation of adult, embryonic and neoplastic brain and meninges

Tissue	Transfer	
	Homologous*	Heterologous
Brain		
Adult human		−
Adult rabbit	+	−
Embryonic human		
Embryonic rabbit	+	+
Mouse glioblastoma	+	+
Human glioblastoma I		+
Human glioblastoma II		+
Human glioblastoma III		+
Meninges		
Adult rabbit	+	+
Adult guinea pig	+	+
Embryonic rabbit	+	+
Embryonic guinea pig	+	+
Human meningioma (fibromatous)		−
Human meningioma (endothelial)		+

* It should be emphasized that the term homologous transfer as used in this paper means transfer to an *unrelated* animal of the same species.

the results obtained are summarized from this viewpoint in Table I. It was found that homologous transplantation was uniformly successful whereas the success of heterologous transfer was dependent on the developmental state of the tissue used. Thus, normal adult brain failed to grow in alien species while embryonic and neoplastic brain survived such transfer. The situation differed with respect to the meninges. Here, normal adult tissue, as well as embryonic tissue, survived heterologous transfer. Tumors, classified histo-

logically as meningiomas of fibromatous type, failed to grow in alien species, but an endothelial meningioma gave rise to takes. These points are of some interest from a biological point of view and will be discussed in more detail following a description of the experiments.

Transplantation of Normal Adult Brain. Homologous transplantation experiments were limited to the rabbit. Fragments of cerebral cortex from the brains of 3 different adult rabbits were transferred to the anterior chambers of the eyes of 28 unrelated animals and takes occurred in 10. In these instances, the transplants remained translucent and pinkish in color in contrast to the white opacity of fragments that were subsequently absorbed. Vascularization occurred early and in less than ten days small vessels derived from the iris could be seen traversing the graft.

The transplants did not increase appreciably in size but remained stationary throughout the period of study. The majority of rabbits were killed for histological examination between the second and third months but several were held under observation for as long as five months without regression of the transplants.

Histologically, sections of the transplants were made up of cells of a single type growing in a solid medullary mass. The cells contained a large amount of finely vacuolated cytoplasm with a relatively small vesicular nucleus and could not be identified with any normal component of the brain (Figs. 1 and 2). In some regions they formed irregular syncytial masses separated by fine connective-tissue stroma bearing thin-walled vessels—while in others individual cell boundaries were discernible. Mitotic figures were scattered sparsely throughout.

Despite the failure to recognize the cell type, available evidence indicates that the cell mass was derived from survival and growth of a neuroglial element contained in the transplanted brain rather than from a reactive proliferation on the part of the host. Comparable cells have not been observed in anterior chamber transplants of other tissues and occurred consistently in the present series.

In contrast to the results of homologous transplantation, no element of the adult brain survived heterologous transfer. A total of 75 guinea pigs (30 and 45 respectively) were used in transfer experiments involving human and rabbit brain and in no instance did the transplanted fragments survive more than a week. During this period there was no evidence of vascularization or growth. On the contrary, the fragments either disappeared completely during the first few days or were obscured by an acute inflammatory reaction.

Transplantation of Normal Embryonic Brain. The homologous transplantation of embryonic rabbit brain was highly successful. In the present series, 46 rabbits were used and takes occurred in 42. It is probable that in the unsuccessful cases, the transplanted fragments escaped through the incision shortly after transfer, for embryonic brain is a slippery, gelatinous substance and is not easily wedged in the inferior angle of the iris.

Growth of the transplants was noticeable within a week of transfer and

continued to fill two-thirds to three-quarters of the chamber in a two months' period. Thereafter progressive growth ceased and no further change in size or appearance was observed. Several of the animals have now been under observation for two and a half years and the transplants show no sign of regressive change.

The transplants may grow as rounded, expanding masses but sometimes show a curious coarse wrinkling suggestive of convolutions and gyri. Not infrequently small fragments of the transplanted material are dislocated from the main graft during the course of transfer and come to lie in scattered positions over the surface of the iris. These give rise to separate foci of growth and eventually coalesce to form a single mass.

Histologically, the transplants show numerous healthy ganglion cells in addition to glial elements (Figs. 3, 4 and 5). In a number of instances, ependymal cells lining a ventricle-like cavity were found (Figs. 6 and 7).

The transplantation of rabbit and human embryonic brain to the anterior chambers of guinea pig eyes also gave rise to a high percentage of takes with progressive growth comparable to that obtained in the homologous transfer of embryonic rabbit tissue. Transfer was successfully effected in 41 out of 43 guinea pigs utilizing rabbit brain and in 50 out of 55 pigs using human brain.

The transplants increased at a slower rate than was noted in homologous transfers but growth continued for a longer period of time. In some cases the fragments grew to fill the chamber and in others remained without further increase after attaining one-half this size. Pigs bearing human brain were followed for more than two years without the appearance of regressive changes and there is no reason to believe that the transplants would not persist throughout the life of the alien host.

Usually all of the transplanted tissue survived transfer and, from the beginning, the uniform expansion of the growing mass could be observed with the naked eye. In a few animals, on the contrary, the bulk of the transplanted material was absorbed or at least disappeared from the chamber within a few days of transfer. Sometimes no trace of the transplant could be found with a magnifying lens and in such instances the impulse was to record the transfer as a failure and to discard the animals. However, in the

PLATE I*

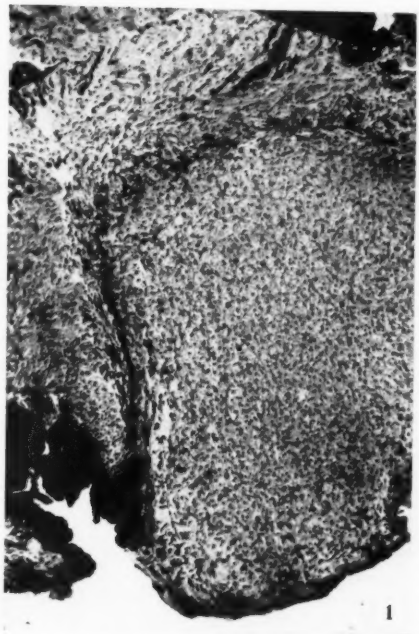
FIG. 1. Homologous transplant of adult rabbit brain. Rabbit bearing transplant was killed two months after transfer. Transplant is demarcated from iris by a narrow zone of pigment-bearing cells. Hematoxylin and eosin, ×85.

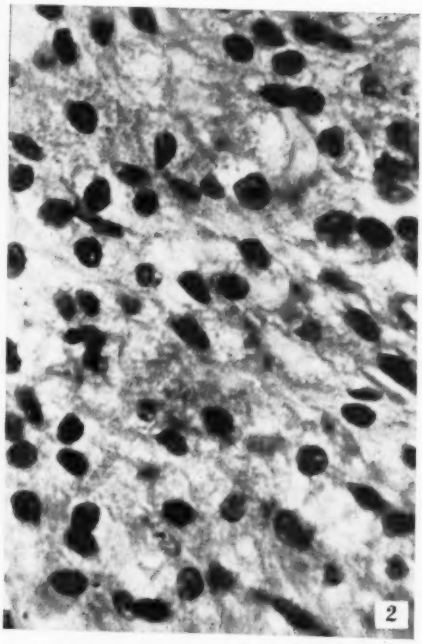
FIG. 2. Higher power view of previous transplant to show character of cells. Hematoxylin and eosin, ×700.

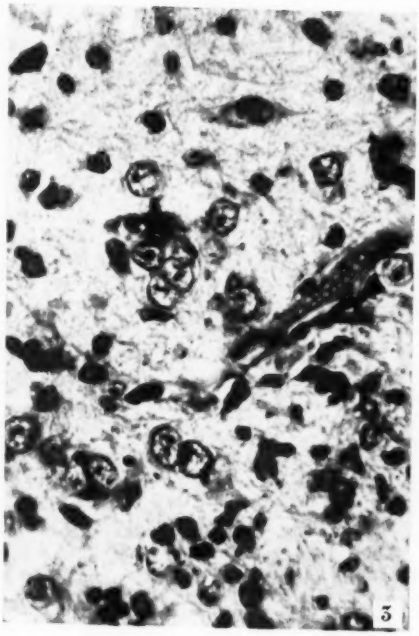
FIG. 3. Homologous transplant of embryonic rabbit brain. Rabbit bearing transplant was killed 161 days after transfer. Note ganglion cells in this and two following photographs. Hematoxylin and eosin, ×500.

FIG. 4. Homologous transplant of embryonic rabbit brain. Rabbit bearing transplant was killed 144 days after transfer. Hematoxylin and eosin, ×600.

* All figures photographed by Mildred L. Konick.







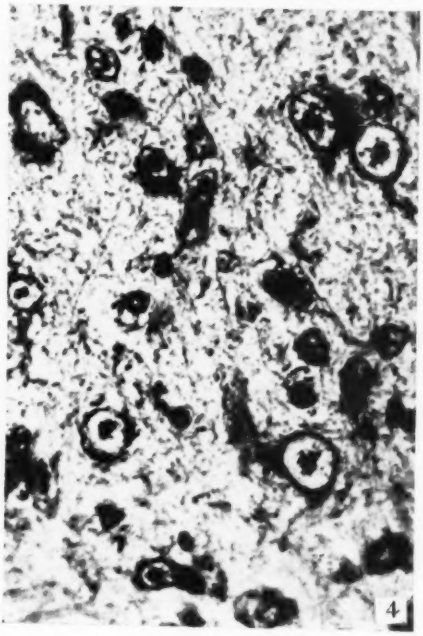


PLATE I

great majority minute foci of growth soon became apparent and often enlarged rapidly. The appearance of such foci was occasionally delayed for long periods of time. In one particular instance of this type, a pig had been released from the experiment as "negative" and transferred to another group for different study. A full year elapsed during which the animal was under constant surveillance and at the end of this period a minute area of growth was observed for the first time.

Histologically, the heterologous transplants appeared in no way different from homologous growths of brain and consisted of well formed ganglion cells and glial elements (Figs. 8, 9 and 10).

Transplantation of Brain Tumors. The homologous transplantability of brain tumors was demonstrated by Zimmerman and Arnold utilizing a methylcholanthrene induced mouse glioma. A comparable growth was obtained in a C_3H mouse, and has been carried by serial subcutaneous transfer in this strain with a high percentage of takes. The tumor has also been found to grow equally well in the subcutaneous tissues of dba mice.

Growth of this tumor was readily obtained in the anterior chamber of the guinea pig. Transplantation experiments using the subcutaneous tumors of six different mice resulted in growth in 36 out of 70 pigs. Serial guinea pig transfer was successfully performed in three instances and, in one case, the tumor was carried for five consecutive generations. The percentage of takes increased with continued passage and growth was obtained in all animals after the second transfer.

The tumor grew rapidly in the guinea pig's eye. Takes were usually evident by the seventh day and the chamber filled by the end of the third week. Thereafter, regression occurred but was followed by renewed growth in five per cent of cases.

Histologically, the transplants showed a more densely cellular structure than the parent mouse tumor but were identical in other respects (Figs. 11 and 12).

Attempts were made to transplant 3 different human brain tumors to the anterior chambers of pig's eyes, and in each instance growth was obtained. The tumors were all classified as glioblastoma multiforme and for convenience of description will be referred to as glioblastoma I, II and III.

Glioblastoma I. This tumor occurred in the right frontal lobe of a thirty-year-old male. Histologically, it was characterized by a striking pleomorphism with large, bizarre, bipolar spongioblasts, protoplasmic astrocytes, astroblasts and a large number of mono- and multi-

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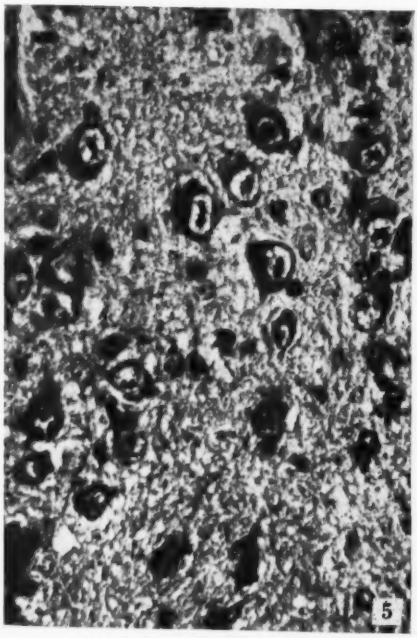
PLATE II

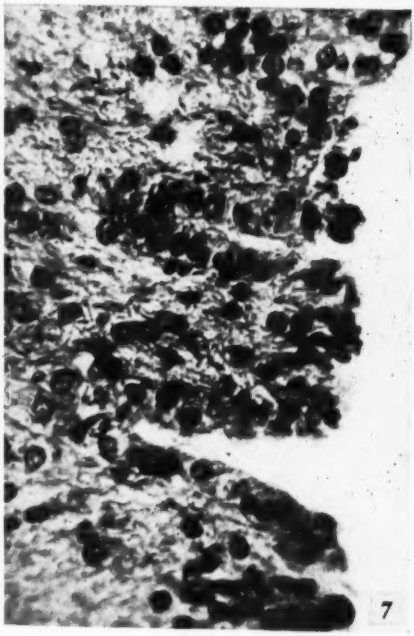
FIG. 5. Homologous transplant of embryonic rabbit brain. Rabbit bearing transplant was killed 556 days after transfer. Hematoxylin and eosin, ×500.

FIG. 6. Homologous transplant of embryonic rabbit brain containing ventricle-like cavity lined by ependyma. Hematoxylin and eosin, ×235.

FIG. 7. Higher power view of previous transplant to show ependymal lining. Hematoxylin and eosin, ×475.

FIG. 8. Heterologous transplant of embryonic human brain. Guinea pig bearing transplant was killed 138 days after transfer. Note ganglion cells. Nissl's stain, ×800.





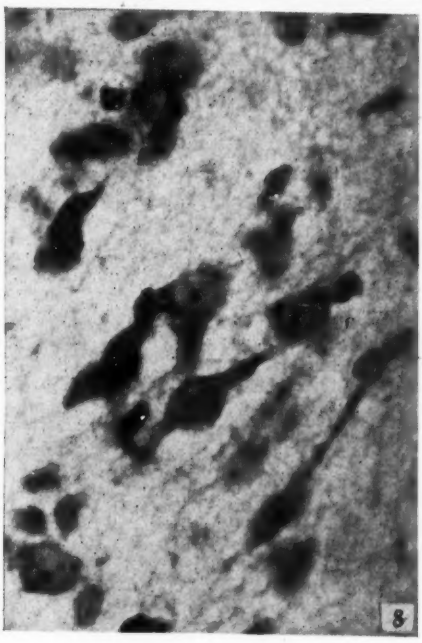


PLATE II

nucleated giant cells. There were numerous mitotic figures and necrosis was extensive. Vascular endothelial proliferation was prominent.

The tumor was stored in the icebox after removal and transfer was not attempted until the next day (twelve hours after operation). Despite this long delay growth occurred.

Six guinea pigs were used in the experiment but the true incidence of takes is uncertain for, on the 100th day after transfer, 3 of the animals were discarded. There was no evidence of growth at this time and, as far as could be determined, all of the transplanted material had disappeared from the eye. The transfer was considered unsuccessful and the guinea pigs were released. Three were killed and the remainder transferred to the breeding colony.

On the 250th day of the experiment, minute foci of growth were observed in the eyes of the 3 breeding animals. They appeared in the region of the iris originally occupied by the transplanted tissue and were at first of such size that their presence was only detectable with a magnifying lens. Subsequent growth was comparatively rapid and by the 288th day the growths had increased to fill one-half to two-thirds of the chambers. At this time the animals were killed for microscopic study of the tumor and further transplantation experiments.

Fragments of the tissue from the eye of one animal were transferred to 6 new pigs to constitute a second generation. The growth history of the tumor in this generation was similar to that in the first. Takes occurred in 4 out of 6 animals but in no case was growth evident before the end of the ninth month. The pigs were killed with their chambers completely filled with tumor one year and eleven days after transfer. A third generation passage was made but it is yet too early to determine the presence or absence of takes.

Histologically, the transplants were identical with the primary tumor (Figs. 13 and 14).

Glioblastoma II. This tumor arose in the posterior right temporal lobe of a twenty-five-year-old female. Microscopically, it was composed largely of protoplasmic and fibrillary astrocytes with few spongioblasts and little endothelial proliferation. However, there were many nuclei in mitosis and several giant cells were found.

Fragments of the tumor were transferred to the eyes of 6 guinea pigs immediately after operation. Takes were observed in 3 of the pigs between the 190th and 220th days and the animals were killed on the 276th day. At

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PLATE III

FIG. 9. Different area of transplant shown in Fig. 8. Nissl's stain, ×900.

FIG. 10. Heterologous transplant of embryonic rabbit brain. Guinea pig bearing transplant was killed 97 days after transfer. Note ganglion cells, glia cells and large giant cell. Hematoxylin and eosin, ×500.

FIG. 11. Homologous transplant of methylcholanthrene induced mouse glioblastoma in subcutaneous tissues of a C_3H mouse. Hematoxylin and eosin, ×275.

FIG. 12. Transplant of tumor shown in Fig. 11 in anterior chamber of guinea pig's eye. Hematoxylin and eosin, ×275.

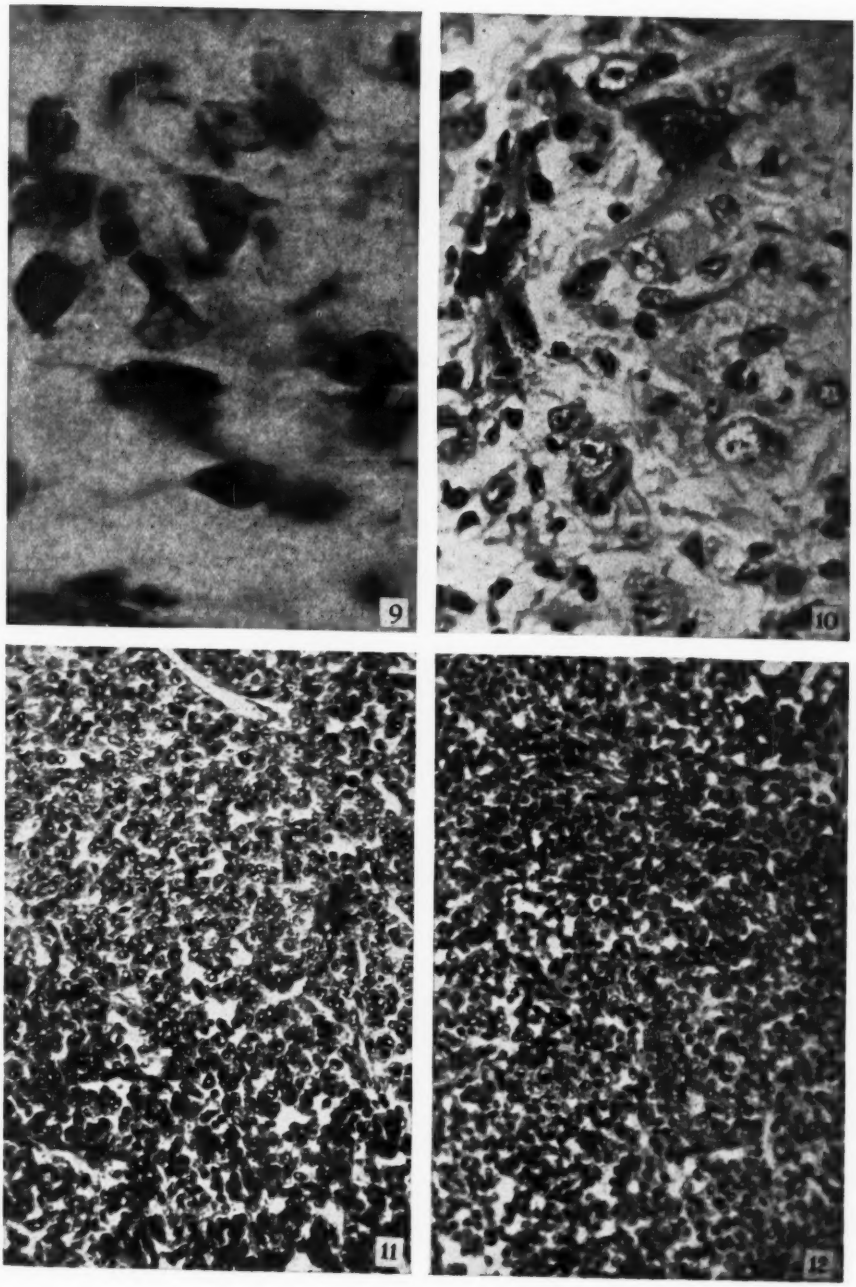


PLATE III

that time, the growths occupied two-thirds of the anterior chamber and were histologically identical with the primary tumor (Figs. 15 and 16).

Glioblastoma III. This growth arose in the right frontal lobe of a sixty-year-old male and on microscopic examination showed the typical cellular morphology and vascular proliferation of a glioblastoma multiforme.

Transfer was performed immediately after operation and takes occurred in 4 of the 6 pigs used. Growth was not evident until the 270th day and when the animals were killed on the 318th day, the tumors occupied one-half to two-thirds of the anterior chamber. Microscopically, they were identical with the primary growth in the brain (Figs. 17 and 18).

Transplantation of Normal Adult Meninges. Experiments with adult meninges were limited to the transfer of rabbit tissues to the eyes of other rabbits and of guinea pigs, and the transfer of guinea pig meninges to the eyes of other pigs and of rabbits. An attempt was made to select pia-arachnoid rather than dura for transplantation but such a separation was usually impossible.

Transfer of rabbit meninges to rabbit eyes resulted in 8 takes in the 10 animals used and a similar proportion was obtained in the homologous transfer of guinea pig meninges (11 out of 15). Heterologous transplantation, surprisingly, also gave rise to takes, although the incidence was considerably lower than that observed in homologous transfer (6 out of 25).

The successful transplants in both homologous and heterologous species showed no observable increase in size and a determination of the outcome of transfer in living animals was based on vascularization and the absence of degenerative changes. Fragments that failed to take became opaque white in color, homogeneous in appearance and either diminished in size or were obscured in an inflammatory reaction. Inflammatory reactions were common in unsuccessful heterologous transfers and rare in homologous experiments. Successful transplants in both heterologous and homologous species remained semitranslucent in appearance and vascularization was evident within a few days of transfer. These features persisted throughout the six-weeks period of observation. It seems significant that in both types of transplantation, takes were more apt to follow the transfer of tissue containing the least dura and the most pia-arachnoid.

Microscopically, the successful transplants were made up of whorl-like arrangements of cells reminiscent of arachnoid villi scattered in a matrix of collagenous connective tissue (Figs. 19, 20 and 21). Unsuccessful transplants,

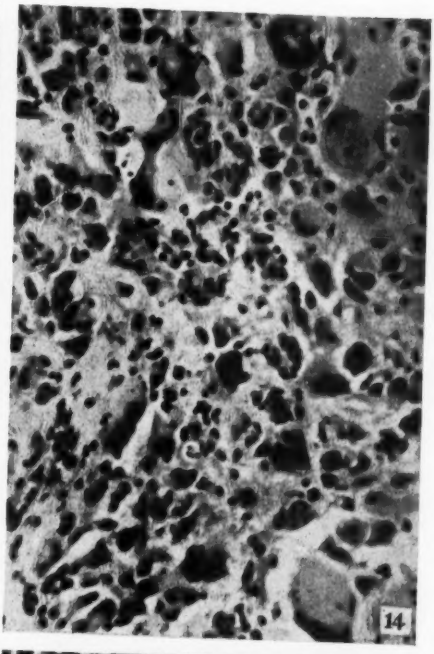
PLATE IV

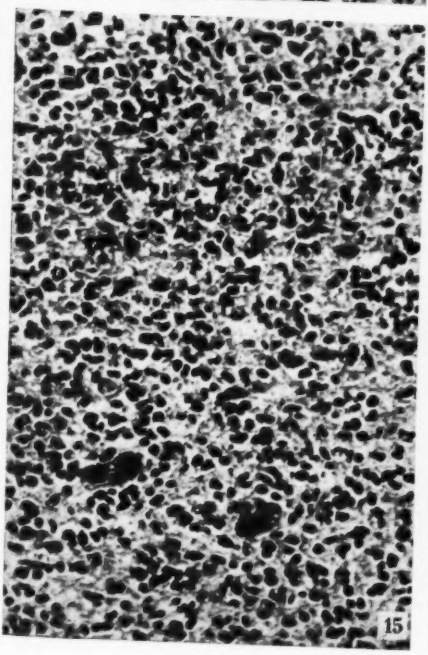
FIG. 13. Human glioblastoma multiforme referred to in text as Glioblastoma I. Hematoxylin and eosin, ×275.

FIG. 14. Heterologous transplant of Glioblastoma I. Guinea pig bearing the transplant was killed 288 days after transfer. Hematoxylin and eosin, ×275.

FIG. 15. Human glioblastoma multiforme referred to in text as Glioblastoma II. Hematoxylin and eosin, ×275.

FIG. 16. Heterologous transplant of Glioblastoma II. Guinea pig bearing transplant was killed 276 days after transfer. Hematoxylin and eosin, ×275.





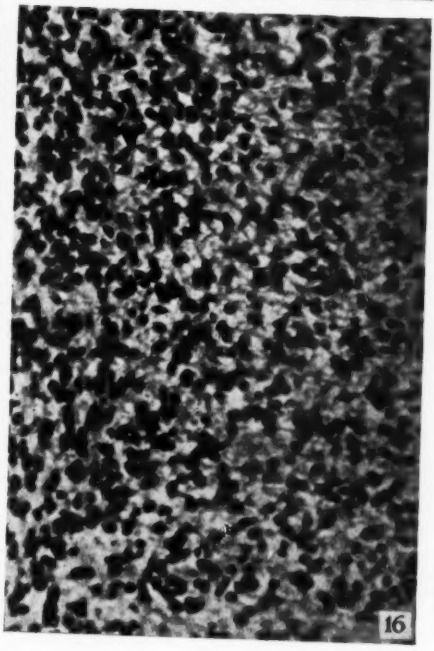


PLATE IV

on the other hand, consisted of hyalinized fibrous connective tissue diffusely infiltrated with inflammatory cells.

Transplantation of Embryonic Meninges. As might be expected from the results recorded above, a high incidence of takes was obtained in the homologous and heterologous transfer of embryonic meninges. The inflammatory reactions encountered in heterologous experiments were not observed despite the fact that no attempt was made to separate the dura from the pia-arachnoid and, with few exceptions, all transplants survived.

Histologically, two types of growth were encountered in both homologous and heterologous transplants. One type consisted solely of connective tissue with areas of hyalinization while the other was distinguished by the presence of whorl-like structures and accumulations of flattened epithelioid cells (Fig. 22).

Transplantation of Meningiomas. The meningiomas used for transfer to guinea pig eyes varied considerably in morphology and the success of transplantation appeared to be directly related to their histological structures. Four of the tumors consisted almost entirely of dense bundles of collagenous fibers, and structures suggestive of an arachnoidal origin were extremely sparse. The fifth tumor, on the contrary, was made up entirely of flattened endothelial cells with vesicular nuclei arranged in a whorl pattern. Variations in nuclear size and mitotic figures were infrequently seen. This tumor represented the third recurrence of a growth originally removed in 1923.

The eyes of 40 guinea pigs were inoculated with fragments of the four fibromatous tumors and the animals were held under observation for six months but in no instance did a take occur. The fragments became opaque white in color, diminished in size and, on section, were found to consist of acellular hyaline connective tissue containing foci of calcification.

On the contrary takes occurred in 4 of the 8 animals used for the transfer of the endothelial meningioma. Growth was evident on the fourteenth day after transfer and during the following month the fragments grew to occupy one-fourth of the anterior chamber. Further increase in size did not occur and signs of regression were present in the transplant of the oldest animal of the series killed on the 241st day.

A second generation transfer was attempted and here also growth occurred in fifty per cent of the pigs used.

Histologically, the transplants were identical with the primary tumor (Figs. 23 and 24).

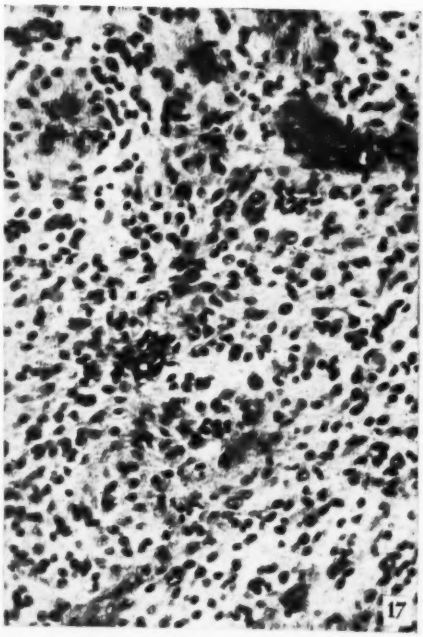
PLATE V

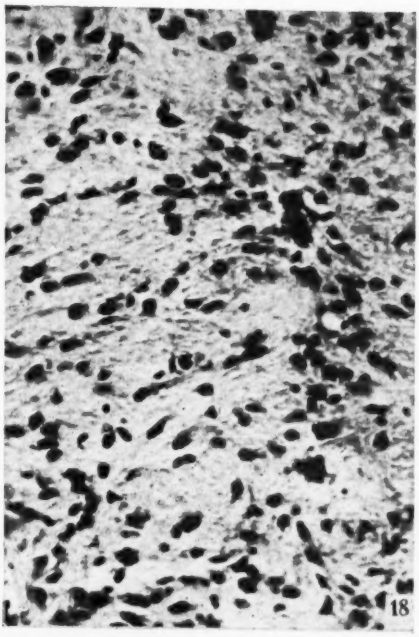
FIG. 17. Human glioblastoma multiforme referred to in text as Glioblastoma III. Hematoxylin and eosin, ×275.

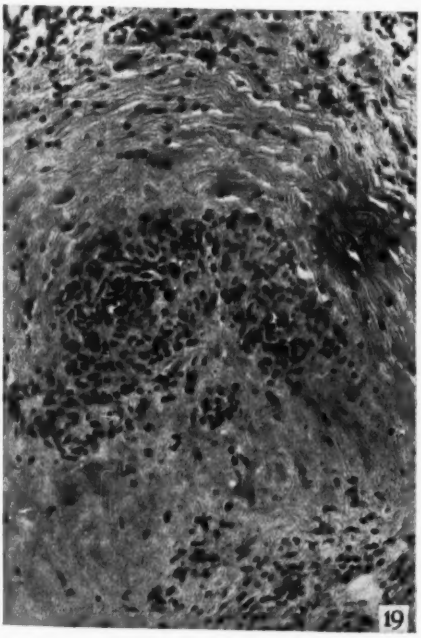
FIG. 18. Heterologous transplant of Glioblastoma III. Guinea pig bearing transplant was killed 318 days after transfer. Hematoxylin and eosin, ×275.

FIG. 19. Homologous transplant of adult guinea pig meninges. Guinea pig bearing transplant was killed six weeks after transfer. Hematoxylin and eosin, ×190.

FIG. 20. Heterologous transplant of adult rabbit meninges. Guinea pig bearing transplant was killed six weeks after transfer. Hematoxylin and eosin, ×275.







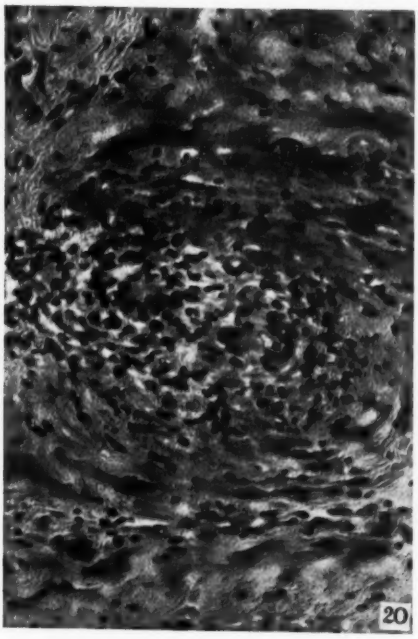


PLATE V

DISCUSSION

As previously noted, the primary object of this paper is to indicate the usefulness of the anterior chamber of the eye in neurological research. Transplantation to this site offers a method of approach to the study of cytogenesis, neoplasia and even of infectious diseases, without the disadvantages incident to the artificial conditions of tissue culture. It should be emphasized in this connection that growth in the anterior chamber does not proceed in the manner of a tissue culture. The transplants rapidly become vascularized and, in actuality, are part of the new host, subject to the stimuli and inhibitions that regulate and integrate the organism, rather than isolated from such influences in a culture flask or roller tube.

The experiments described in this paper were undertaken as part of a general survey of body tissues with reference to heterotransplantability but the results obtained in relation to the nervous system suggest that an extension in this direction with more detailed observations might contribute directly to several outstanding neurological questions. The ability of embryonic brain to grow and to differentiate offers a ready means for investigating the developmental potencies of different areas, the effects of early disorganization of the cortex and a multiplicity of other problems requiring easily accessible growths of isolated brain substance. Further, the accessibility of the transplant and the ability to alter its constituents experimentally suggests a possible application of the procedure to the study of electroencephalography.

The growth and development of human embryonic brain in lower animals is of interest from several points of view. It constitutes a possible approach to the transmission and cultivation of infectious neurotropic agents that exhibit a specificity for human brain and have not been successfully transferred to lower animals. Further, it affords a means of testing the reaction of human tissue to chemical substances known to exert a carcinogenic effect in the brain substance of lower species.

The existence of human brain in lower animals also excites speculation from a purely philosophical standpoint. On the assumption that the human brain is the seat of the intellect, some alteration might be expected in the behavior of guinea pigs bearing such transplants. However, observation has shown no change suggestive of higher faculties. In fact, the only variation differentiating a guinea pig bearing a human brain from a normal pig is a marked increase in libido.

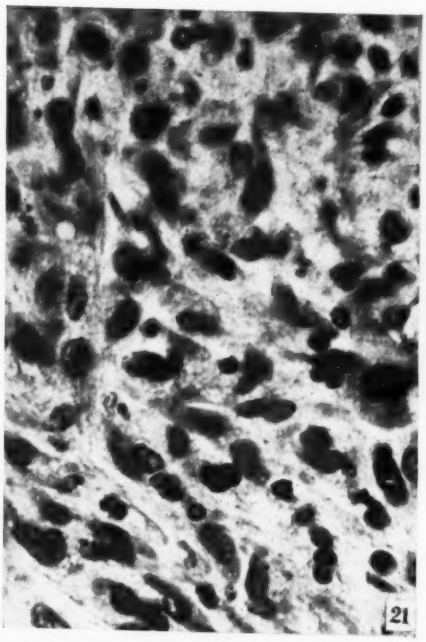
PLATE VI

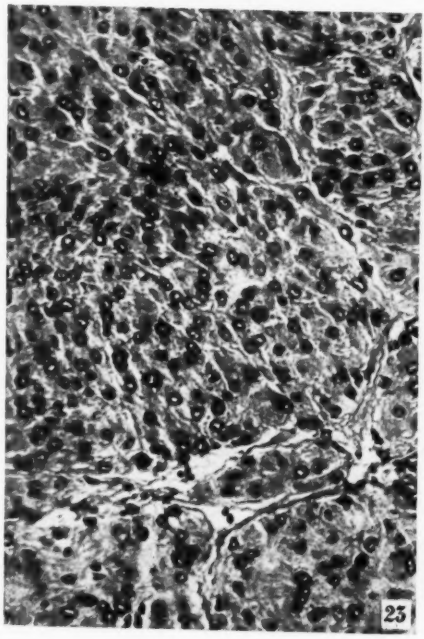
FIG. 21. Higher power view of cellular area in heterologous transplant of adult rabbit meninges. Note mitotic figure. Hematoxylin and eosin, ×650.

FIG. 22. Heterologous transplant of embryonic rabbit meninges. Guinea pig bearing transplant was killed 50 days after transfer. Hematoxylin and eosin, ×275.

FIG. 23. Human meningioma of endothelial type. Hematoxylin and eosin, ×275.

FIG. 24. Heterologous transplant of endothelial meningioma shown in Fig. 23. Guinea pig bearing transplant was killed 241 days after transfer. Hematoxylin and eosin, ×275.





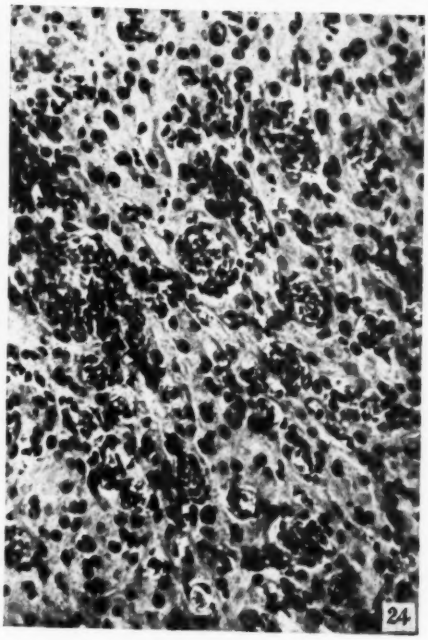


PLATE VI

The successful homologous transplantation of adult brain and the failure of heterologous transfer is in line with results obtained with other organs and tissues. However, the growth of a single unclassified cell and the disappearance of normal cell types in homologous brain grafts is contrary to experience with other organs where all of the component cells and characteristic structures are reduplicated in the transplant. Conceivably, this may be related to the extreme susceptibility of neural elements to anoxia and, unlike the parenchyma of other organs, such elements fail to survive the oxygen deprivation incident to transfer. Accordingly, the surviving cells, constituting the growing transplant, may represent a proliferation of some more resistant glial form.

It is of interest in passing to note that ganglion cells were present in transplants of embryonic brain despite the long period of anoxia between transfer and vascularization. It is possible in this case, however, that neural ectoderm or some other precursor less susceptible to oxygen lack survived transfer and subsequently underwent normal development to ganglion cells.

The growth of adult meninges in heterologous species was also contrary to experience with adult tissues. Other adult tissues, with the significant exception of the sheath of Schwann, have not survived such transfer. The heterologous transplantation of Schwann's sheath will be reported in the next paper of this series, but the analogous behavior of this tissue and the pia-arachnoid appears of sufficient interest to warrant present mention. The origin of Schwann's sheath from the neural crest is generally accepted, but the demonstration by Harvey and Burr of the neural crest origin of the pia-arachnoid is disputed by some workers.[4] The present experiments offer contributory evidence of an indirect nature. The behavior of the two tissues on heterologous transfer differentiates them from other parts of the body and the possession of common growth properties peculiar to these tissues and not shared by others suggests a close relationship of a genetic as well as a biological order.

Further evidence of such a relationship may be adduced from the heterologous transplantation of tumors of the two tissues. An extensive survey of the heterotransplantability of the benign tumors of nearly all tissues has been completed and only those of Schwann's sheath and the pia-arachnoid have been successfully transferred to alien species.

The heterologous transplantation experiments involving meningiomas are of interest from another viewpoint. Four of the tumors were fibromatous in character, contained only traces of arachnoid structures and were not transplantable. The fifth tumor was predominantly arachnoid in character, contained little fibrous connective tissue and was readily transplantable. Somewhat similar results have been obtained in the heterologous transplantation of scirrhous and medullary breast cancers and lead to the suggestion that the fibromatous tissue in meningiomas may represent a desmoplastic reaction comparable to that found in scirrhous carcinoma.

The ability of the glioblastomas to survive and to grow in animals of

alien species is a property held in common with the malignant tumors of other organs and tissues and, from the standpoint of autonomy, identifies these growths with the ordinary sarcomas and carcinomas. The failure of glioblastomas to metastasize, therefore, cannot be related to an absence of the biological attribute of autonomy but, on the other hand, would appear to be associated with some peculiarity in brain structure or chemistry. The ability to transfer the growths to other sites in foreign hosts brings the problem into the field of experimentation and pertinent investigations are in progress.

Such investigations are necessarily slow due to the growth behavior of the transplanted tumors. In each instance, transfer was followed by a period of six to nine months during which the transplants remained dormant and without observable change. This latent period was succeeded by rapid growth and, in a relatively short time, the transplants increased to a considerable size. The long interval of dormancy is apparently a characteristic of the glioblastomas. Nearly all other malignant tumors show some evidence of growth before the end of the second month and occasionally, as in the recent case of a chordoma, fill the chamber in three weeks. A long latent period, often four to five months, characterizes the growth of malignant melanomas, a point of some interest in view of the possible nervous origin of these tumors.

SUMMARY

The experiments reported in this paper were concerned with an investigation of the transplantability of adult, embryonic and neoplastic brain tissues including the meninges in homologous and heterologous species, utilizing the anterior chamber of the eye as a transplantation site. Homologous transfer was uniformly successful and transplants of brain and meninges in various developmental states survived and grew in animals of the same species. As in the case of other organs and tissues, adult brain failed to grow in alien species whereas embryonic and neoplastic brain survived such transfer. The situation differed with respect to the meninges, and normal adult tissue as well as embryonic tissue survived heterologous transfer. Meningiomas of fibromatous type failed to grow in alien species but an endothelial meningioma was successfully transferred from man to guinea pigs. These results and the possible application of the method to neurological research are discussed.

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FORWARD NEUROSURGERY IN ITALY

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O.C. Mobile Neurosurgical Unit

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THIS REPORT analyses 700 consecutive neurosurgical cases admitted to a detachment of a mobile neurosurgical unit situated at the Casualty Clearing Station level in the Italian campaign. The work covers the 9 months' period from the beginning of the campaign to midsummer of 1944 as the 8th Army was advancing up the Adriatic coast.

In this sector of the front the lines of communication were long and narrow, and evacuation to the base was by rail only. Air evacuation, so successfully employed on the other side of Italy and now from Western Europe, could not be provided due to the nature of the terrain. For this reason it was not possible to place a unit in such a position that it could both hold cases for a reasonable length of time after operation and at the same time receive them early enough to minimize the ever-present danger of sepsis. Thus, as in the campaign in the Middle East (Eden, 1943), the unit was split into two operating teams, a forward detachment attached to a forward C.C.S. and a rear section at the base hospital level to receive and hold casualties operated on by the forward section. For the most part this arrangement functioned according to plan.

A COMPOSITE SPECIAL TEAM

The idea of specialist teams working together in close collaboration in the forward areas was first conceived by the administrators of the 8th Army in the Middle East, where the neurosurgical and ophthalmic units were usually attached to the same C.C.S. Later on this combination was further augmented by the addition of the maxillo-facial team. Thus at the beginning of the Italian Campaign there existed a composite team made up of a mobile ophthalmic unit and the forward detachments of the neurosurgical and maxillo-facial units. The same arrangement of special units held good at the base, where the rear sections of the neurosurgical and maxillo-facial units and an eye surgeon all worked in the same base hospital. At the base section were received the casualties from the forward detachments, as well as many battle accidents occurring along the lines of communication and patients from the Jugoslav theatre of operations. This "Trinity," although consisting of 3 separate units, was always considered as one large special team which, as the Army advanced, moved from parent unit to parent unit in its effort to receive battle casualties as soon as possible after wounding. This composite team was attached to the C.C.S. which most conveniently drained the whole battle front, i.e., the most forward bottle-neck C.C.S. In most situations, the casualties arrived within 24 hours; in others, depending on the rapidity of the advance and the condition of the roads, the time interval was longer.

The average time interval between wounding and operation in this series was 27.6 hours (maximum 5 days—minimum 6 hours).

The advantage of having the forward special units together are fairly obvious. In the first place, the sorting of casualties by the medical officers farther forward is facilitated: all patients with wounds above the neck are immediately evacuated direct to the special teams. In the second place, many of the wounds are of such a nature that they require treatment by two or more of the special surgeons. The fact that these surgeons are in the same place obviates the necessity of harmful transportation, discontinuity of treatment and multiple anaesthetics in patients who are, not uncommonly, dangerously ill.

THE C.C.S. AS A PARENT UNIT

Casualty clearing stations, to which the units were attached, in every case were accommodated in buildings, usually schools or monasteries. In some instances, due to limitations of space, all the teams were obliged to work in one large operating theatre, but it was found that they functioned more efficiently when separate theatres were provided.

There are certain disadvantages under which special units attached to a C.C.S. must necessarily work. These are due to the fact that the C.C.S. is a mobile structure, transports its own equipment, which therefore cannot be elaborate, and must adapt its equipment and the accommodation provided to fulfil its needs. Thus the X-ray and laboratory facilities are limited and cannot attain the standard that exists in a base hospital. The patients, unless dangerously ill, cannot be held for more than 2 or 3 days and must be evacuated to make room for more casualties, and this also applies to head cases. In rush periods, beds are at a premium, and at times it is necessary to nurse dangerously ill patients with head injuries, and even patients with complete spinal cord lesions, on stretchers on the floor.

Nevertheless it was felt that these disadvantages were outweighed by one paramount factor: the patients were given the benefits of complete operation early, with the result that in a large percentage of cases the long drawn-out treatment of intracranial infections with their attendant dire consequences was eliminated.

PERSONNEL AND OPERATING FACILITIES

The neurosurgical component of the "Trinity" consisted of one surgeon and an operating staff of three. One ward sister, well trained in the difficult art of handling postoperative neurosurgical cases, was found to be almost indispensable. Too much cannot be said for the khaki-clad nursing sisters who cheerfully work in the forward areas, often under very bad conditions. One anaesthetist was shared by the three units. In battle periods this led to situations in which he would often have 3 and occasionally 4 anaesthetics under way at one time. He must needs be an adept and experienced anaesthetist. In order to circumvent this difficulty to some degree, regional block anaesthesia, using 1 per cent novotox, was employed in 56 per cent of pene-

trating brain wounds and nearly all non-dural penetrating wounds. Usually in these cases a basal narcosis was induced, using alopon, gr. ½, scopolamine, gr. 1/150 and luminal, gr. 3. Thus, what was considered to be the anaesthetic of choice in suitable head cases became the anaesthetic of necessity in many other cases which would have been more satisfactorily dealt with under general anaesthesia.

The procedure adopted with regard to combined neurosurgical and general surgical cases was as follows. Provided that it was the major wound, the neurosurgeon first dealt with the head wound, using local anaesthesia, after which the patient was returned to the general preoperative ward and was placed on the appropriate priority list for the general surgeons. This, of course, required the cooperation of the general surgeons, which was readily forthcoming at all times. The arrangement, although seeming superfluous to persons who have not been privileged to observe a C.C.S. in action under battle conditions, was considered to be most satisfactory, since it allowed each surgeon to deal with his own cases in their proper priority and at his own convenience.

Since the personnel and equipment on the establishment of a mobile neurosurgical unit does not provide for the splitting of the unit into two sections, considerable adaptation was necessary. This applied more particularly to the personnel, as a considerable amount of captured enemy equipment was acquired and utilized. On several occasions as many as 30 to 40 neurosurgical patients were lying in the preoperative ward at once. One surgeon only was available to sort the wheat from the chaff and dispose of the chaff, do a preoperative neurological examination on the patients who required operation, operate on them, write up the notes on the field medical card, as well as keep unit records, care for them postoperatively, and arrange their evacuation. However in periods of "normal" activity, this burden was lessened considerably and one surgeon was able to cope readily with the situation.

The team was admirably equipped with instruments and in addition possessed a diathermy apparatus and sucker. These special accessories, together with the lighting, were powered by a 4 kilowatt petrol generator. Of all the special facilities required to perform an adequate debridement of a brain track, satisfactory lighting was considered to be the most important. This was provided, in the case of this unit, by a captured German spotlight using a 100 or 200 Watt bulb. It was adjustable and could be "spotted" to light up any required part of even the deepest brain tracks. The next most important item of equipment was the sucker, without which it was impossible to do any deep work. The diathermy was useful but not essential. Bleeding was not severe in the majority of brain tracks, and haemostasis could be secured by means of hot saline sponges. During a long period when the generator broke down, the diathermy was not available and it was necessary to use a foot sucker—an old tire pump with the valve reversed. This answered very well as a substitute.

The sterilizing was done by primus stoves in the operating theatre. Rarely was there sufficient space for a separate sterilizing room.

One table was used for operating while a stretcher placed on two trestles served as a preparation table.

PRIORITY OF CASES

The sorting process usually eliminated about 30 per cent of the casualties labelled "neurosurgical." These were either very minor head wounds, with or without other lesions that required the attention of the general surgeons, or deeply comatose patients with severe brain wounds, who were placed in a low operating priority because of their poor prognosis occasioned by gross cerebral destruction. Of the remaining cases, minor injuries with absent or minimal neurological signs were first dealt with. These patients were evacuated immediately following operation and it was not unusual, when the ambulances were running a continuous shuttle service, to have them operated on and evacuated within 2 hours after admission to the C.C.S. Then followed the more severe penetrating wounds in order of their severity. Finally the "bad" lesions were again reviewed and the more hopeful operated on.

Analysis of Cases

British	250
Canadian	217
Indian	129
New Zealand	49
Miscellaneous (Prisoner-of-War, Italian Army of Liberation, Polish, etc.)	55
Total	700

The various types of cases are recorded below. The usual classification is used, i.e. those involving scalp only, those involving bone, and those involving brain.

1. Brain wounds	239
2. Bone involved—dura intact	127
3. Scalp wounds	299
4. Spines	24
5. Miscellaneous	11
Total	700

It was not possible to evacuate all the patients with non-dural penetrating wounds to the base neurosurgical team and consequently no follow-up on these is available. Of 239 penetrating brain wounds, due to missiles, operated on by the forward section of the unit, follow-ups are available on 217. The great majority of these passed through the rear section of the unit. The average length of follow-up is 42 days. Brain wounds were 34.1 per cent of the total.

The following figures refer only to the series of 217 in which follow-up records were obtained.

Site of Brain Wound

1. Cerebral hemispheres	140
2. Orbital and frontal sinus	12
3. Frontal sinus—no orbital involvement	17
4. Mastoid and petrous bone	8
5. Through & through brain wounds	13
6. Ventricular wounds	27
Total	217

The great majority of patients arriving at the forward detachment of the neurosurgical unit had had no previous treatment except possibly a shaving of the scalp around the wound and application of sulpha powder. This non-intervention policy forward of the neurosurgical team was the result of instructions issued by 8th Army Medical authorities and was eminently satisfactory. Reoperating on a patient who has had the scalp wound excised and sutured with silk worm gut increases by ten fold the difficulties of the neurosurgeon who must re-excise the scalp wound and furthermore close it. As previously stated, C.C.S. X-rays, particularly of special regions such as the skull and spine, do not provide the detail that one sees in those taken by static base units. However, reasonably good anteroposterior and lateral views were usually available, showing the position of the metallic foreign bodies and bone chips, but little information as to the number of chips. Occasionally operation had to be performed without preoperative X-rays, and in these cases good debridements were usually obtained. Preoperative X-rays, then, are desirable but not absolutely essential as a preliminary to the adequate debridement of a brain wound.

The principles of treatment of these wounds have already been described. The object aimed at was to debride the brain track thoroughly and remove all bone chips and the metallic foreign body if possible. Rarely was a bone flap necessary for penetrating wounds: the whole operation was performed through the defect caused by the missile. No large area of bone in the vicinity of the wound was ever removed for decompression purposes. Scalp flaps were often necessary to effect closure of the wound in two layers: sharply angled points were avoided if possible in the scalp closure. The wounds were not drained. A firm plaster of Paris head cap was applied in all cases, even scalp wounds, and upon this was written the diagnosis, date of operation and date for removal of the stitches. Temporal wounds tended to develop subcutaneous collections of fluid in the dead space caused by the removal of temporal muscle and the contraction of the remaining muscle fibres contributed to it. Several cases of mild trismus were observed in these patients.

Fascial grafting of the dural defect was resorted to only infrequently in the uncomplicated brain wounds. Recently some ventricular wounds and

wounds involving the paranasal sinuses have been grafted at the primary operation with satisfactory results.

PENICILLIN

Penicillin was used in a majority of the cases. It was applied locally to the wound in the form of a calcium powder combined with sulphanilamide or sulphathiazole powder. Usually the proportion was 1000 units penicillin to 1 gram of the powder, but for one period powder containing 5000 units penicillin per gram was used. In periods when penicillin was not available, sulphathiazole powder was used. No routine use was made of parenteral or intrathecal penicillin in the forward area.

INFECTIONS

In the whole series of brain wounds, infection occurred in 28 cases. This represents an infection rate of 12.9 per cent of the total. If the deaths due to primary brain destruction are deleted from the total, the figure is 13.9 per cent. Although sulphathiazole powder alone was used in only 32 cases, a comparison of the infection rate between those wounds treated with penicillin combined with a sulpha drug and those treated with sulphathiazole alone shows a very striking difference in favour of penicillin. A statistical expert who was consulted stated that the difference in the healing rate of the two groups of cases was "highly significant."

Drug used	No. cases	Infections	%
1. Penicillin & sulpha drug.	184	17	9.2
2. Sulphathiazole	32	10	31.2
3. No local application	1	1	—
Totals	217	28	12.9

This overall figure of 87.1 per cent of primary healing without complicating infection contrasts very favourably with the corresponding figure of 71.6 per cent obtained by this same unit in the Middle East where sulphathiazole only was used locally (Eden). These figures demonstrate the already established fact that penicillin applied locally is a powerful barrier to the development of wound infection. Routine systemic sulphadiazine was a constant factor in both series. The above facts become even more significant when one considers the climatic factors involved. In Italy, as opposed to the desert, pathogenic organisms were more constant inhabitants of the soil and consequently of the wounds. This was demonstrated by the higher frequency with which sepsis occurred in untreated wounds in Italy. As the majority of the above patients were wounded during the Italian winter with its now

famous slush and mud, the sepsis rate would be expected to be on a higher level than in the desert with its clean sands and hot, dry climate.

Types of Infection

Type of infection	Total	Early	Late	Deaths	Treated by	
					Penicillin	Thiazole
1. Abscess	11	7	4	5	10	1
2. Meningitis	8	7	1	6	2	6
3. Encephalitis	1	1	0	1	0	1
4. Anaerobic	2	2	0	1	1	0
5. Fungus (uncomplicated)	3	1	2	0	2	1
6. Superficial only	3	1	2	0	2	1
Total	28	19	9	13	17	10

An infection classified as "late" in the above table is one which became manifest more than 10 days after operation. Fungi were also present in many cases otherwise classified.

Three of the abscesses occurred around metallic foreign bodies remote from the entrance wound. This phenomenon was not observed in the Middle East series, where no effort was made to remove the foreign body unless easily accessible. However, more recently, since these infections have occurred, more attention has been paid to the removal of the metal.

Two of the patients with abscess indicate the need for long-term follow-up in the evaluation of sepsis rate. One had been perfectly well with a healed retracted wound for 5 weeks. After his routine lumbar encephalogram he failed to recover as expected and the X-rays showed a space-occupying lesion of the brain under his skin wound. A large amount of sterile pus was evacuated by aspiration through the wound and thorotrast inserted for radiological visualization of the abscess cavity. This was repeated until the abscess had shrunk to about one-third its original size as shown by radiographs. He is now perfectly well and awaits removal of the fibrous capsule. The other patient, also with a healed skin wound, developed Jacksonian seizures 2 months after operation, and a large loculated abscess was evacuated. His wound later healed by granulation.

The high mortality in cases complicated by meningitis can partly be explained by the fact that these patients had all been on full doses of sulphadiazine since operation, but despite this had developed meningitis. The armamentarium of treatment was exhausted, since it was before the days of intrathecal and intraventricular penicillin therapy.

MORTALITY

The mortality rate has very little significance since it depends on the time interval between wounding and arrival at the C.C.S. The farther forward the

unit was stationed, the higher the mortality rate became, because more of the severely wounded reached the unit alive but moribund. Many patients in this category who arrived in rush periods were not operated on. Had these patients arrived in a slack period, they would probably have been operated on with the same fatal results due to gross brain destruction.

In this series 32 deaths occurred, i.e., 14.7 per cent of the patients operated on. Fourteen of these died of infections of various types, i.e., 6.4 per cent of the total. Most of the others died of primary brain damage. One man died 10 weeks after injury of bronchopneumonia with no sign of intracranial infection at post mortem, although he had had a severe wound with a large fungus which had become completely epithelialized.

SUMMARY

1. A series of 700 neurosurgical patients operated on by the forward detachment of a mobile neurosurgical unit in Italy has been analysed. Comments are made on the accommodation and facilities provided for the unit and some of the difficulties encountered.

2. A forward composite specialist team which operated at the Casualty Clearing Station level is described. This team consisted of a mobile ophthalmic unit, and the forward detachments of a mobile neurosurgical and a maxillo-facial unit.

3. Principles of treatment of penetrating brain wounds are briefly outlined.

4. Primary healing of penetrating brain wounds due to missiles in this series was 87.1 per cent.

5. The sepsis rate in brain wounds was significantly lower when penicillin powder was applied locally at operation than when sulphathiazole powder was used.

I wish to tender my sincere thanks to all the members of both forward and rear sections of the unit for their efficient co-operation at all times and to Brigadier Hugh Cairns, Consultant Neurosurgeon to the Army, for his encouragement and criticism in the preparation of this paper.

SUBDURAL HYGROMA

A REPORT OF SEVEN CASES

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THE SUBDURAL SPACE still remains an unsolved mystery in medicine. The anatomical details and studies of the subdural space are meagre indeed.[13,22] Penfield made anatomical studies of the subdural space in dogs and estimated the contents to be a few drops to one cc. per kilogram. Estimations of the normal amount of fluid in the subdural space in humans have not been made, many neurosurgeons feeling that no subdural fluid is normally present. Operations at the vertex of the skull obviously fail to reveal the fluid because of its gravitation to the base. This basal subdural fluid has been repeatedly shown to me by Dr. Temple Fay[9] in his Gasserian ganglion operations by the transtemporal approach. By nicking the subtemporal dura, large quantities of subdural fluid well out of the wound, insuring ample and easy approach to the Gasserian ganglion.

The origin of excessive subdural fluid accumulations, designated subdural hydroma by Dandy,[8] has likewise created heated controversies. Dandy has listed three causes. Trauma is the foremost cause, resulting in arachnoidal tears with leakage of cerebrospinal fluid into the subdural space; secondly, subdural effusions may arise secondary to infection of overlying bone, as in mastoiditis; and thirdly, accumulations are occasionally seen secondary to a communicating hydrocephalus with tearing of the arachnoid at the basal cisterns. Most neurosurgeons believe that excessive collections of subdural fluid are the result of tearing of the arachnoid, the rent acting as a ball-valve mechanism preventing the return of the cerebrospinal fluid to its original confines. Adson[7] was fortunate to observe such a tear in the arachnoid in one of his cases. All cases of traumatic subdural fluid effusions are probably not due to a tear in the arachnoid. McConnell's[17] case No. 7 was quite interesting. The first drill opening made 7 hours after injury failed to reveal any subdural fluid while 9 days later, on re-exploration, a copious stream of yellow subdural fluid was evacuated despite repeated spinal fluid drainages. If a tear in the arachnoid were responsible for the subdural collection in this case, it should have been found at the first exploration. The author has had a similar experience (see Case 7).

The pathology of the fluid removed has likewise offered difficulties since gross contamination with blood occurs when the dura is opened. However, the protein content as reported by various investigators varies from 30 to 5000 mgm. per 100 cc. The fluid is variously described as clear, xanthochromic, or blood-tinged. The amount may vary from 30 cc. to 2300 cc. (Cohen's case[6]).

HISTORICAL REVIEW

The first descriptions of post-traumatic subdural hygromas were written by Professor Payr[21] of Germany during the first World War in 1916. His original descriptions under the name of meningitis serosa traumatica are complete in every detail. Little has since been added to his classical work in the *Medizinische Klinik*. He reported 4 cases: one occurring in the frontoparietal area, two over the temporal lobe and one in the posterior fossa. These four cases were due to tangential bullet wound injuries of the skull.

Dr. Charles Mayo[19] in 1894 operated upon a brain cyst which undoubtedly appears to be a true subdural hygroma. Dr. Naffziger's report[20] of 1924 was important as it stimulated a growing interest in this condition among neurosurgeons in this country. He discussed the etiology and symptomatology, and outlined the most rational treatment for the condition.

In 1927 there appeared the interesting report by Ira Cohen.[6] He described a case in which a massive accumulation of subdural fluid had caused displacement and compression of the brain with focal and increased intracranial pressure symptoms.

With the exception of the writing of Dandy[8] in 1932 in Dean Lewis' *Practice of Surgery*, a decade had passed before interest was again revived by the reports of the Mayo group (Love[15] in 1937, Walsh and Shelden[27] in 1937, and Da Costa and Adson[7] in 1941).

In England, the first and perhaps most extensive report was that of Adams McConnell[16] in 1941. His 32 cases were well described and verified by operation. He divided them into 4 groups: Group 1—patients whose condition was deteriorating, usually within 48 hours of injury and characterized by an expanding lesion (8 cases); Group 2—patients who were in the process of recovery from definite general cerebral contusion, but in whom full recovery seemed to have been checked—passive space-occupying lesion (6 cases); Group 3—patients suffering from headache, dizziness, and vague symptoms of nervous instability dating from a head injury (4 cases); and Group 4—patients in whom headache and occasionally some definite nervous symptom, constant for the individual, started some time after a head injury —best operative results (12 cases).

In 1942 Scott[23] reported 3 cases of prolonged stupor associated with subdural hygromas and in the following year he[24] described a case of acute subdural hygroma which simulated the syndrome of an extradural hemorrhage. Sirois[25] in 1942 reported a case in a 9-year-old boy which was successfully treated surgically. In the following year Ley, Roca de Vinals and Sard[14] wrote on collections of the subdural space.

With the advent of World War II an interesting group of subdural effusions secondary to blast concussion has been described by Abbott, Due and Nosik.[1,2,3] These authors reported a total of 37 cases stressing, in particular, the psychiatric symptoms and the pre- and postoperative responses to standard psychometric examinations. Haynes[11] added three more case reports in *War Medicine* in 1944. In the same year, McConnell[18] added 5 cases

of post-traumatic amnesia due to subdural hygromas. All cases were verified by operation.

Table I outlines the clinical features of the cases reported up to the present time including the author's seven cases. All of McConnell's cases are not included but only the most significant and detailed case was chosen from each of the four groups.

CASE REPORTS

Case 1. Mr. R. J., age 45, admitted August 1944.

Patient was struck in left temporal area with handle of a compressor hammer. Rendered unconscious immediately. Seen immediately following the accident but presented no focal

FIG. 1. Case 1. Encephalogram. Obliteration of subarachnoid channels over both hemispheres. A bilateral subdural hygroma was disclosed at operation.

signs. X-rays of the skull were normal. He had headache, however, and was instructed to return on the following day. Somewhat improved for the next three days, but headache persisted and therefore he was admitted for observation. Lumbar puncture: spinal fluid clear; pressure 10 mm. of Hg. Following this procedure the headache improved and he was discharged.

Oct. 8, 1944. Readmitted because of return of generalized headache and weakness of left arm. Grip notably diminished on left. Marked fatigue and nervousness. Deep tendon reflexes slightly increased on left. Fundi normal. Re-examination of skull by roentgenography showed the pineal gland to occupy a normal position. Blood counts, urinalysis and serology were normal.

TABLE I

Author	Age	Sex	Unconsciousness	P.R.	B.P.	Focal Symptoms	Pupils	Other Cerebral Symptoms	Increased Intracerebral Pressure	Spinal Fluid	Subdural Fluid	Roentgenograms	Surgery and Results
Mayo 1894	11	M	6 wks.	—	—	+	Lt. dilated	Headache, aphasia, hemiplegia, 25 convulsions.	Bulging dura	—	4 oz. clear fluid	—	Unilateral trephine. Rapid recovery.
Payr 1916 4 cases	—	M	—	—	—	+	—	—	—	—	500 cc.	—	Punctured corpus callosum.
Cohen 1927	20	M	None	46, –	—	+	Equal	Headache, aphasia, dizziness, vomiting, convulsions.	Papilledema 4D	Pressure +, xanthochromic, 70 lymphocytes	2300 cc., 9 drainages, xanthochromic	Large air cavity	Right subtemporal decompression. Recovery.
Love 1937	34	F	5 mins.	70, –	110/74	+	Argyll-Robertson	Headache, belligerent, irritable, poor memory.	—	Protein, 90 mgm. %, + Wassermann, Gold curve 5555333210, 37 lymphocytes	Protein, 160 mgm. %, + Wassermann	Encephalogram, incomplete vnetricular filling, absence of subarachnoid markings	Unilateral trephine. Good recovery.
Walsh and Shelden 1937	9	M	1–2 hrs.	60, 15	90/60	+	—	Drowsy, restless, irritable.	Tense dura	—	90–120 cc. slightly bloody fluid	Normal skull	"English" decompression. Good recovery.
Da Costa & Adson 1941	9	M	1–2 hrs.	—	—	+	—	Drowsy.	Tense dura	—	4 ozs. blood-tinged cerebrospinal fluid	Normal skull	"English" decompression. Good recovery.
McConnell 1941 32 cases Group 1 Case 6	48	M	10 days	140, 60	90/78	+	Rt. dilated	Semi-comatose, bilateral grasp reflex.	Tense dura	3 cc. yellowish fluid, protein 40 mgm. %	1 oz. on rt., less on lt., dark yellow fluid, protein 180 mgm. %	—	Bilateral trephines. Expired.
Group 2 Case 7	22	M	10 days	40–50	—	0	Rt. larger than lt.	Stupor followed by hyperexcitable state, dementia.	—	—	Considerable blood-stained fluid	Stellate fracture rt. parietal bone	Right temporal trephine. Good recovery.
Group 3 Case 11	40	M	Some hrs.	—	—	0	—	Headache, dizziness, nervous instability.	—	—	Considerable clear fluid on rt., none on lt.	Depressed fracture, rt. parietal bone.	Right parietal decompression. Left trephine. Good recovery.
Group 4 Case 16	33	M	Stunned an instant	50, –	—	0	—	Left-sided headaches, tiredness, inability to concentrate.	Ventricular pressure 100 mm. Hg.	—	Free flow of clear fluid 24 hrs. after operation	Normal ventriculogram	Left temporal trephine. Good recovery.
Sirois 1942	9	child	24 hrs.	—	—	+	—	Aphasia, hemiplegia.	Tense dura	—	300 cc. blood-tinged xanthochromic fluid, protein 100 mgm. %	—	Trephine. Recovery.

TABLE I—*Continued*

Author	Age	Sex	Unconsciousness	P.R.	B.P.	Focal Symptoms	Pupils	Other Cerebral Symptoms	Increased Intracerebral Pressure	Spinal Fluid	Subdural Fluid	Roentgenograms	Surgery and Results
Scott 1942 Case 1	1	child	5 days after convulsion	—	—	+	Lt. dilated	Aphasia, stupor, choreiform movements.	—	18 cc. moderately bloody fluid	4 ozs. clear fluid	Linear fracture lt. frontal bone	Unilateral trephine. Good recovery.
Case 2	19	M	26 days	100, 20	120/80	+	Equal	Prolonged stupor, restlessness.	Tense dura	Clear fluid	3 ozs. clear fluid rt., 1 oz. clear fluid lt.	Fracture rt. orbit and lt. frontal bone	Bilateral trephines. Good recovery.
Case 3	69	M	48 hrs.	90, 16	120/70	+	Miotic (morphine)	Prolonged stupor.	—	—	3 ozs. golden fluid rt., 3000 mgm. %; 4 ozs. golden fluid lt., 5000 mgm. %	Fracture lt. temporal bone.	Bilateral trephines. Good recovery.
McConnell 1942 Case 1	22	M	19 hrs.	130, 0	110/65	0	Pinpoint	Semi-coma, corneal reflex loss, Cheyne-Stokes respirations.	—	—	Clear fluid	—	Unilateral trephine. Expired.
Case 2	8	F	20 hrs.	96, 38	—	+	Equal	Semi-coma, hemiplegia	Pressure not recorded on manometer	Blood-stained fluid	Yellowish fluid spurted lt., small amount rt.	Circular fracture lt. parietal and occipital bones	Bilateral trephines; re-exploration of left wound, more fluid. Recovery.
Case 7	52	M	7 hrs.	60–70	—	+	Rt. dilated, fixed	Confusion, incontinence.	None	Blood-stained; pressure 100 mm. H_2O	Copious yellowish stream, both sides	Fracture sphenoid bone and orbital roof, obliteration of subarachnoid air shadow	Negative exploration, 7 hrs. after injury; 9 days later large subdural effusion. Recovery.
Case 12	12	M	1 hr.	70, –	105/75	0	—	Headache.	Increased	180 mm. H_2O	Large amount clear fluid bilaterally, protein 2000 mgm. %	—	Bilateral trephines. Good recovery.
Scott 1943	9	M	1 hr.	—, 6	—	+	Miotic then dilated	Jacksonian convulsions, stupor.	Tense dura	Pinkish fluid, pressure 12 mm. Hg.	2 ozs. clear fluid	Transverse fracture frontal bone	Unilateral trephine. Good recovery.
McConnell 1944 5 cases Case 6	42	M	4½ hrs.	44, –	—	0	—	Amnesia, confused.	—	Blood-stained fluid, pressure 135 mm. H_2O, protein 30 mgm. %	93 cc. on rt., 200 cc. on lt., protein 180 mgm. %	Normal skull	Bilateral trephines. Recovery.
Case 22	23	M	Hazy 24 hrs.	—	—	0	—	Headache, dizziness, dullness, lack of sense of responsibility.	—	Protein 30 mgm. %	Large amount bloody xanthochromic fluid on lt., small amount on rt.	Obliteration of subarachnoid patterns on both sides	Bilateral trephines. Improved.

Haynes 1944 Case 1	63	F	No history of trauma	—	—		—	Hallucinations, delirium.	2D rt., secondary optic atrophy lt.	Normal pressure, normal analysis	Large amount xanthochromic fluid	No ventricular distortion. Lack of subarachnoid patterns over lt. frontal lobe.	Left frontal craniotomy. Partial recovery.
Case 2	22	M	3 days	144, 32	160/110	0	—	Prolonged stupor.	None	Pressure 120 mm. H_2O	5 ozs. clear fluid	Normal	Bilateral trephines. Good recovery.
Case 3	25	M	Duration?	—	—	—	—	Coma.	—	Not done	200 cc. on rt., negative on lt.	Multiple basilar fractures	Bilateral trephines. Expired.
Abbott, Due & Nosik 1943 7 cases	24	M	2 days	72, –	130/80	—	—	Headache, vertigo, loss of memory.	Yes	Pressure 200 mm. H_2O, protein 30 mgm. %	Left subdural effusion	Encephalogram, filling defect lt. lower temporal area	Unilateral temporal trephine. Good recovery.
Abbott, Due & Nosik 1943 25 cases Case 7	38	M	Dazed several days	—	—	0	—	Syncope, ataxia, impaired hearing, irritability, inability to concentrate.	—	Protein, 35 mgm. %	Large rt. subdural hematoma, large lt. subdural effusion	—	Bilateral trephines. Good recovery.
Wycis 1944 7 cases Case 1	45	M	1½ hrs.	60–80	120/80	+	Equal	Headache, hemiparesis, irritability.	None	Slightly xanthochromic, pressure 8 mm. Hg., protein 100 mgm. %	3 ozs. xanthochromic fluid on rt., 1 oz. on lt. Protein 4000 mgm. %	Obliteration of subarachnoid pathways. No ventricular distortion	Bilateral trephines. Incomplete recovery.
Case 2	23	M	Duration?	50, 16	100/60	0	Equal	Apathetic, headache, drowsiness, dizziness.	2D on lt., 2D on rt.	Not done	Large amount blood-stained fluid on both sides	No shift of midline structures	Bilateral trephines. Complete recovery.
Case 3	13	M	Momentary	80, 20	—	—	Equal	Restlessness, maniacal, profane.	Normal fundi	Clear fluid, pressure 10 mm. Hg.	Moderate amount xanthochromic fluid on rt., less clear fluid on lt.	Stellate depressed fracture, temporal and sphenoid bones on rt.	Bilateral trephines. Complete recovery.
Case 4	28	F	Duration?	75, 18	100/60	—	Equal	Headache, nervousness.	None	Normal pressure and analysis	2 ozs. clear fluid bilaterally	Subarachnoid fibrosis	Bilateral trephines. Good recovery.
Case 5	8	F	About 1 hr.	80, 20	100/60	+	Equal	Aphasia, hemiplegia, intermittent stupor, restlessness.	None	Mild xanthochromia, pressure 10 mm. Hg.	Xanthochromic, ¼ oz. on lt., ½ oz. on rt.	—	Bilateral trephines. Complete recovery.
Case 6	43	M	1 hr.	—	—	—	Equal	Headache, pain over rt. eye, irritability, nervousness.	Normal fundi	Clear fluid, pressure 10 mm. Hg., protein 35 mgm. %	3–4 oz. xanthochromic fluid, protein 117 mgm. %	Obliteration of subarachnoid patterns on rt. side	Bilateral trephines. Complete recovery.
Case 7	42	M	?	—	—	+	Rt. dilated	Drowsiness, hemiparesis, restlessness.	—	Bloody fluid, pressure 10 mm. Hg.	Large amount xanthochromic fluid on rt., less on lt.	Fracture rt. temporal bone.	Three trephines. Complete recovery.

Oct. 11. Encephalogram (Fig. 1). Obliteration of the fluid pathways over the convex surfaces of both hemispheres. Normal filling of ventricular system without any displacement. Headaches appeared to be aggravated by encephalography. Normal spinal fluid analysis.

Oct. 17. Bilateral exploratory trephines—local anesthesia. Two trephines made over premotor areas. On opening dura on the right, there was an immediate gush and spurt of slightly yellowish fluid. When the dural incision was enlarged, at least 3 to 4 ozs. of subdural fluid were evacuated. On the left side a similar pathology was seen except that the subdural fluid was less in amount. At completion of procedure the brain was pulsating and had fallen away from the undersurface of the dura so that two rubber tube drains could be easily introduced into the subdural space.

Oct. 18. Condition markedly improved. Free of headache. Definite return of power in left arm and forearm. Dressing profusely wet. Fluids forced orally. Subdural fluid contained 4000 mgm. per cent of protein.

Oct. 29. Patient discharged symptom-free.

Comment. Of striking interest is the fact that the ventricles, on encephalography, showed no displacement in spite of the existing left monoparesis. Obliteration of the subarachnoid patterns was helpful in the diagnosis. The headaches appeared immediately following the injury while the monoparesis was delayed in onset, suggesting a possible delayed occurrence of the subdural hygroma.

Case 2. Mr. V. McK., age 23, admitted Oct. 14, 1944.

In severe automobile accident in August 1944. Not unconscious. Following this he began having "dizzy spells" which he said were like a "hangover." The spells subsided but returned two weeks following the injury. The attacks were accompanied by malaise and bilateral supraorbital headache. Intermittent diplopia started two months later.

On admission: Temperature 98.8°F.; pulse 48; respirations 16. No localizing signs. Weakness of the left sixth nerve. Bilateral papilledema of 2 D. Roentgenograms of the chest and skull were normal except for an airless right maxillary antrum. Blood counts, urinalysis, sedimentation rate and serology were normal.

Oct. 17. Bilateral exploratory trephines—local anesthesia. Because of the papilledema and absence of localizing signs with previous history of trauma, it was decided to make bilateral exploratory burr openings over the premotor areas. If the pathology could not be discovered by this procedure, it was decided to tap the ventricle from this position and proceed with ventriculography. Accordingly, the burr openings were made over the premotor areas. The dura was tense but not discolored. On nicking the dura, clear subdural fluid spurted out. Approximately 4 ozs. of clear subdural fluid were obtained from each side. An attempt was made to tap the right frontal horn of the lateral ventricle. The ventricle was collapsed and only 5 cc. of fluid could be obtained. A small amount of air was introduced and the cannula withdrawn. Two rubber tube drains were placed to the subdural space. The ventriculogram was indeterminate but some air was seen between the hemispheres, indicating a normal position of the midline structures.

Oct. 18. Alert and conscious. Free of all headache. The pulse had increased from 48 to 80 and the respirations from 16 to 22. The dressing was quite wet on both sides, indicating profuse subdural drainage.

Oct. 23. Symptom-free except for mild diplopia. Papilledema had receded to 1 D. in each eye.

Oct. 29. Discharged symptom-free. Mere blurring of nasal disc margins. Diplopia had subsided. He was seen at two-week intervals for five months. The optic discs were normal. He was back at work as an electric welder and symptom-free.

Comment. Here was an interesting problem of papilledema without localizing signs appearing after a head trauma which was unattended by loss

of consciousness. The small collapsed ventricles should caution one against ventricular puncture in these cases.

Case 3. T. S., age 13, admitted Nov. 9, 1944.

Patient was struck by an automobile and rendered unconscious momentarily. While in the receiving ward he was uncontrollable, restless, and resisted all attempts to aid him. A fractured right radius was also present. There were no localizing neurological signs at this time except for an equivocal Babinski on the right.

On admission: Temperature 96°F.; pulse 80; respirations 20. Spinal fluid pressure 6 mm. of Hg.; fluid blood-tinged.

The outstanding feature was the complete change of personality. He was restless, profane, insulting and unkind. He had a particular dislike for doctors and nurses. The mental reaction, at times, was almost that of a manic psychosis. His cries would awaken the entire ward. For the first three days he slept almost continuously, but could be aroused readily. His mother stated that prior to the accident he was a most model and polite gentleman.

On the third day he was re-examined for any focal neurological signs. The subgaleal hematoma was diminished in size but still fluctuant. The pupils were miotic but equal, responding sluggishly to light. There was mild impairment of facial movements on the right which may have been due to the contusion over the right cheek. The extremities were moved freely. The deep tendon reflexes were active and equal. Babinski and Hoffmann signs could not be elicited.

Nov. 15. Spinal puncture: pressure 6 mm. of Hg.; 20 cc. of clear fluid slowly removed. X-ray of skull: stellate fracture in the right temporal region involving greater wing of sphenoid bone. There was a considerable depression of fragments. An additional linear fracture was seen in the right parietal bone with some separation of the parieto-temporal suture.

Nov. 16. Severe change in personality persisted. Refused medication, resisted examination. Very profane. Masturbated before ward personnel. Complained of headache and cried as does a spoiled child.

Nov. 17. Bilateral exploratory trephines. The incision on the right was made over the temporal area just anterior to and above the ear. On separating the periosteum from the bone a large gush of chocolate-colored fluid, approximately 3 ozs., escaped from the subgaleal collection. The temporal bone was fractured in several places and there was a marked indentation in the sphenoid ridge with depression of the temporal lobe. The fragments were elevated and removed piece-meal by rongeur. A small epidural collection of clotted blood was removed by suction. A large collection of clotted blood was seen beneath the temporal muscle dissecting the muscle free from the periosteum. This was likewise removed by suction. One large, loose fragment of bone, which extended to the base of the skull, was not removed for fear of serious bleeding.

The dura was tight and not discolored. A moderate amount of clear yellow subdural fluid escaped on incising the dura. The drainage increased with manipulation of the head and retraction of the brain by means of a brain spoon. The underlying cerebrum appeared normal. A drain was placed through the temporal muscle and dura, to the subdural space.

A single burr opening on the left showed a tight dura. There was likewise a moderate amount of subdural fluid present but on this side it was clear and colorless. One tube drain was placed in the subdural space.

Nov. 18. There was noted a marked and sudden change in personality. He was quiet, took his medication, and refused to swear. He permitted examination. He ate solid food for the first time during his illness. There was an amnesia for his past episodes of profanity and misbehavior. The head dressing was quite wet from subdural fluid drainage.

Nov. 19. He permitted a change of his dressing and removal of the subdural drains.

Nov. 21. Out of bed. Eating and feeling well. Apologetic for his past behavior.

Nov. 24. Discharged symptom-free except for moderate emotional instability and increased psychomotor activity.

When seen 6 weeks later he was nearly normal except that he still showed an increased psychomotor activity and a tendency to be quite talkative.

Comment. The marked improvement in personality following drainage of the subdural fluid was quite dramatic. Psychotic episodes are not uncommon with subdural hygromas. McConnell cites a patient who required commitment but who fortunately was trephined in time. The result was excellent.

Case 4. Mrs. N. H., age 28, admitted Dec. 2, 1943.

Eight years previously she was in an automobile accident. She was rendered unconscious and was hospitalized for an indeterminate period. Details of the injury could not be recalled. Shortly following the accident she complained of severe pain over the vertex of the skull. She became subject to intermittent headaches which started in both temporal areas, finally becoming generalized. The headaches were aggravated by noises and excitement. The neurological examination was entirely negative. An encephalogram, performed on a previous admission, revealed a normal ventricular system but a failure to completely visualize the subarachnoid patterns.

Dec. 4. Bilateral exploratory trephines—avertin-local anesthesia. The dura was full but not tense. On opening the dura a large amount of clear fluid was seen to escape. By rotating the head and depressing the cortex with a brain spoon, approximately 3 to 4 ozs. of clear fluid were obtained from each side. On the right a cortical vein was inadvertently opened and profuse bleeding occurred which was controlled by cautery.

Dec. 5. Complete relief of headache. There was a moderate weakness of the left foot presumably due to the bleeding from the Rolandic vein.

Dec. 14. Discharged. Symptom-free. Foot drop markedly improved.

She was seen at four-week intervals for the next 8 months. She felt well but still had occasional headaches in the temporal areas.

Comment. In this case there were prolonged headaches without focal neurological signs, due to a chronic bilateral subdural hygroma. Relief was almost complete with surgical drainage of the subdural space.

Case 5. Miss P. H., age 8, admitted May 3, 1944.

Eight days prior to admission she was struck by a truck while crossing the street and immediately lost consciousness. She regained consciousness at a near-by hospital, but a right hemiplegia and motor aphasia were recorded. Spinal puncture showed frankly bloody fluid. Two days following the injury she became quite drowsy but could be aroused. Six days later spinal puncture was repeated and the cerebrospinal fluid was xanthochromic. Following this procedure she became more alert and spoke a few coherent words. Periods of alertness would alternate with periods of stupor. Seven days after the injury the respirations became irregular and the pulse rate slowed to 52. On the next day she was transferred to the neurosurgical service at Temple University Hospital.

Examination on admission: Temperature 100°F.; pulse 60; respirations 16. The blood pressure was 104/66. She was drowsy and yet quite restless. A contusion was noted over the left eye and there was a mild degree of ptosis on this side. Her speech was limited to whining and crying. Occasionally a word or two could be spoken. The pupils were equal at 4 mm. and the response to light was prompt. There was a central type of facial weakness on the right. There was marked weakness of the right arm but the lower extremity on this side showed slight paresis. Bilateral Babinski responses could be easily evoked. A hematoma was present over the right clavicle and was due to an underlying fracture. The spinal fluid pressure was 10 mm. of Hg.; 16 cc. of straw-colored fluid were slowly withdrawn. There was a linear fracture of the left parietal bone.

May 5. Bilateral exploratory trephines—avertin-local anesthesia. On the left side the dura was tight but not markedly discolored. On opening the dura a large amount of xanthochromic fluid squirted out under pressure. Approximately 3 ozs. of fluid were removed. A single tube drain was placed to the subdural space. On the right side a similar pathology was found but

the amount of subdural fluid was less, approximately 1 oz. A similar drain was placed to the subdural space.

May 6. She was lucid and alert. She said "yes" and "no." The dressing was profusely wet from the drains in the subdural space.

May 8. Restlessness markedly subsided. Speech was still explosive but the words could be said with less difficulty.

May 11. Hemiparesis diminished markedly. She was able to form short sentences.

May 12. Able to count and form sentences.

May 15. Marked improvement in the aphasia. Now able to carry on a limited conversation. Hemiparesis had completely cleared but there was ataxia of both upper limbs, particularly on the right.

May 18. Discharged. She was seen at two- and three-week intervals for the following eight months. She is totally well and attending school. Her grades are above the average. She plays the piano well.

Comment. Prolonged stupor, and restlessness, with focal neurological signs (aphasia and hemiparesis), were the outstanding features due to a bilateral subdural hygroma. Complete relief of symptoms followed drainage of the subdural space.

Case 6. Mr. J. W., age 43, admitted Jan. 30, 1945.

A month before admission he was struck over the right fronto-temporal area with a heavy piece of lumber which fell from a height of 25 feet. Duration of unconsciousness was one hour. He was hospitalized at another institution and remained there but four days. During his hospital stay he had right-sided headaches and pain down the left arm. His headaches persisted and became increasingly severe. There were likewise irritability, nervousness, tremor and memory impairment. A semi-circular scar was present on the right frontal area. This was extremely sensitive to touch. The left eye was artificial. There were no localizing neurological findings.

Jan. 31. Encephalogram (Fig. 2). The initial spinal fluid pressure was 10 mm. of Hg.; protein was 35 mgm. per cent. A subdural air shadow was seen over the right cerebral hemisphere. There was a failure of visualization of the subarachnoid patterns over the left cerebral hemisphere. No shift of midline structures. The right lateral ventricle did not fill, but the left lateral ventricle had a normal appearance.

Feb. 3. Bilateral exploratory trephines—avertin-local anesthesia. The dura was not tense or discolored. When the dura was opened on both sides, a stream of clear xanthochromic fluid in copious amounts (3 to 4 ozs.) welled out of the wound. The brain fell away from the dura and was seen to freely pulsate. Rubber tube drains were placed in the subdural space and fluid was seen to pulsate in the ends of the rubber tubes at the completion of the procedure.

There was an immediate marked amelioration of all symptoms. The headache, tremor and nervousness had completely abated. Because of profuse drainage, the drains were allowed to remain for 3 days. The patient had been given sulfadiazine prophylactically (1 gm. every 4 hours) two days preoperatively and 5 days postoperatively. The subdural fluid contained 117 mgm. per cent protein.

Comment. The encephalogram indicates a drainage of the subdural space on the right side and yet the spinal-fluid protein was but 35 mgm. per cent, while the subdural fluid obtained at operation was 117 mgm. per cent. The case is of interest in that it demonstrates how typical post-concussional symptoms may be relieved by drainage of the subdural space.

Case 7. Mr. H. T., age 42, admitted Oct. 10, 1943.

He was seen to fall from the top of a machine into a pit below, a distance of some ten feet. He was apparently not unconscious and was able to climb a ladder out of the pit without sup-

port. Vomiting immediately ensued. He was immediately taken to the emergency admission ward at Temple University Hospital. He was quite euphoric and insisted that he was well. At that time the pupils were equal and responded promptly to light. There were four lacerations about the right ear and occipital area. A bloody cerebrospinal fluid leak from the right ear was noted. Spinal puncture: pressure 10 mm. of Hg.; fluid bloody. Within half an hour the right pupil dilated and the left side became paretic. Drowsiness followed. An emergency right temporal exploratory trephine was carried out. A transverse fracture line was noted running almost parallel to the squamous suture of the temporal bone. The trephine opening was made below the fracture line. When the bone was removed a small epidural hemorrhage

FIG. 2. Case 6. Encephalogram. Note the obliteration of the subarachnoid spaces on the right and the presence of the subdural air shadow on the left. The left ventricle failed to fill but the right showed no displacement. A bilateral subdural hygroma was disclosed at operation.

was present. The dura was blue and tense. On opening the dura chocolate-colored clots of blood escaped from the wound. These were evacuated by irrigation and suction with a soft rubber catheter. The brain was tight and herniated into the wound, indicating an already existing intrinsic cerebral edema. Two drains were placed in the subdural space. At the completion of the procedure the pupils were nearly equal and responded promptly to light.

During the next three days he still had an incomplete left hemiplegia. Spinal puncture was repeated. The pressure was low and 5 cc. of xanthochromic fluid were removed. Because drowsiness and restlessness had increased, bilateral exploratory trephine openings were made in each parietal area. The dura was slightly discolored. On opening the dura, a large amount of subdural xanthochromic fluid escaped. There was more subdural fluid on the right side than on the left. Drains were placed in the subdural space. Drowsiness and hemiplegia per-

sisted for three days. The right pupil was larger than the left and did not respond to light. Gradually, the hemiplegia cleared, restlessness subsided and he made a nearly complete recovery.

Three months later he was back at his former occupation. One year later his only difficulty was a slight impairment in concentration and a tendency to tire at the end of the day.

Comment. Persistent drowsiness and focal neurological signs subsided after bilateral drainage of the subdural space. It is notable that the subdural hygroma occurred some time after the first operation and was responsible for the stormy convalescence.

INCIDENCE OF SUBDURAL HYGROMAS

Regarding the frequency of occurrence of this pathological entity, there are few statistics. The best are those of McConnell,[16] who reported subdural effusions in 32 out of 63 patients operated upon for head trauma. Certainly the incidence is higher than has been heretofore suspected.

The frequency is higher in males than in females, most likely due to the severity of occupation and engagement in the theaters of war (blast effusions). In reviewing the cases reported in the literature, there were 26 males and 5 females. The ages varied from 1 to 69 years. The greatest incidence appeared in the second decade of life (9 cases).

The total number of cases is tabulated below:

Author	*Number of Cases*
Mayo, 1894	1
Payr, 1916	4
Cohen, 1927	1
Love, 1937	1
Walsh and Shelden, 1937	1
Da Costa and Adson, 1941	1
McConnell, 1941	32
Sirois, 1942	1
Scott, 1942	3
McConnell, 1942	4
Scott, 1943	1
Abbott, Due and Nosik, 1943*	7
Abbott, Due and Nosik, 1943*	27 (37 less 10 of 1st report)
McConnell, 1944	5
Haynes, 1944	3
Wycis, 1945	7
Total	99 cases

* The subdural effusions and hematomas are not separated in the reports of Abbott, Due and Nosik, hence the total number of subdural hygromas is less than the total number listed above.

SYMPTOMATOLOGY

A history of injury (direct or blast) is usually available. There follows a period of unconsciousness which may vary from moments to weeks. The cases associated with blast concussion may show only an initial state of "daze" which may progress to confusion

Headache, dizziness, nervousness, irritability, restlessness, inability to concentrate, loss of memory, confusion, focal neurological signs (aphasia, hemiparesis, hemiplegia, dilated pupil), drowsiness, semi-coma, and prolonged stupor are frequent post-traumatic symptoms.

In reviewing the detailed case reports of the literature, the following statistics were available when these symptoms were reported. The total number of cases reviewed was 33.

Symptoms	*Number of Times Recorded*
Headache	12
Dizziness	5
Nervousness and irritability	7
Loss of memory and confusion	6
Restlessness	4
Aphasia	5
Hemiparesis or hemiplegia	6
Drowsiness	4
Semi-coma	3
Stupor	7

Headache appears to be the most frequent symptom. It may commence immediately at the time of injury or may make its appearance months later. The headache is usually generalized but may be unilateral and more pronounced on the side of the greatest effusion. Altering head posture may aggravate the headache, particularly when the patient bends forward. The exact mechanism of subdural headache is unknown; however, it is believed to be due to a dural stretch by the entrapped fluid. The marked and dramatic relief following drainage of the subdural space would appear to substantiate this theory. The headache may be temporarily relieved by repeated spinal drainages; however, it is occasionally made worse due to the inability to empty the subdural space with further retraction of the brain from the dura.

Dizziness is likewise a frequent and often persistent symptom following cerebral concussion. It may be the sole symptom for years; however, it is usually associated with the above-named symptoms. The dizziness is usually of an indefinite nature; however, in some cases, a true turning sensation may be described by the patient. In none of the author's cases was a true nystagmus or a true directional vertigo recorded. The causes for post-traumatic vertigo are not definitely known. Spiegel[26] believes that this type of vertigo is the result of vasomotor disturbances of the brain as well as the labyrinth. The sudden increase of intracranial pressure at the instant of concussion is transmitted to the labyrinth as well as other parts of the skull and this impairs vestibular function. This theory is substantiated by the observations of Brunner.[5] After concussing the skulls of guinea pigs he found circulatory disturbances, diapedesis, and transudation of fluid into the endo- and perilymphatic spaces of the inner ear (otitis interna vasomotorica). According to McConnell[17] this symptom is usually the result of cerebral contusion and remains unaltered despite surgical drainage of the subdural hygroma. The

statistical studies of Friedman, Brenner and Denny-Brown[10] attempted to show that there was remarkably little evidence that post-traumatic dizziness was related to vestibular damage. It is often difficult to decide whether dizziness is psychogenic or organic. In such instances it is frequently necessary to determine the presence of a lesion of the labyrinth or the vestibular pathways. Brunner[5] found in uncomplicated post-concussional vertigo lack of marked cochlear disturbance with a normal or increased labyrinthine excitability. Baumoel and Marks[4] were able to show a difference in tonus between the two labyrinths, there being a directional preponderance to one side.

Nervousness and irritability were recorded in seven instances of the 33 cases reviewed. Restlessness was recorded in but four instances. However, the author feels that this symptom has a greater incidence than would appear from statistical analysis.

Loss of memory, confusion and amnesia are not uncommon. In an interesting paper by McConnell,[18] six cases of prolonged post-traumatic amnesia were found to be due to subdural effusion in five instances. McConnell suggested the following sequence of events: "Concussion caused a lengthy period of anoxemia; during this period a subdural effusion developed, interfered further with cerebral function and so prolonged the existing amnesia. The duration of amnesia may be regarded as a measure of the sums of the effects of the initial injury plus subsequent interference with cerebral function." Following blast concussion, Abbott, Due and Nosik[3] reported a high incidence of confusion, memory loss and lowered responses to the Hartford Shipley Retreat and Rorschach tests.

Occasionally the patient becomes delirious, disoriented and even maniacal so that commitment to an asylum has been necessary.

Focal neurological signs are frequently present. These are usually a hemiparesis or hemiplegia associated with or without aphasia. In the blast concussion group and the amnesic group reported by McConnell, focal neurological signs were sparse.

Pupillary anomalies are important signs. The presence of a dilated pupil on the side of the largest effusion is a good operative indicator. A dilated pupil was recorded in but 6 instances of the 33 cases reviewed. Bilateral miosis was recorded in 3 instances.

Occasionally, one may see the classical triad of headache, vomiting and papilledema, thus mimicking a brain tumor (see Case 2).

DIAGNOSIS

As a rule, in the acute cases, the differentiation from a subdural hematoma is difficult and can be settled only by trephining the skull. The persistence of headache, vertigo, irritability, memory impairment and mental confusion after the acute stage of a cerebral trauma has passed should suggest the possibility of a subdural hygroma. The appearance of headache some weeks or months later is not uncommon. Prolonged stupor was par-

ticularly emphasized in the reports of Scott.[23,24] Post-traumatic amnesia as a result of subdural effusion has been stressed by McConnell.[18] The diagnostic characteristics of subdural effusions following blast concussion are mental confusion, absence of localizing signs, and a diminished response to psychometric tests.

In the acute cases, the subdural effusion may act as an expanding lesion, thus mimicking a subdural hematoma. In the chronic cases, the subdural effusion acts as a passive space-occupying lesion, delaying recovery. The persistence of symptoms or delay of recovery following a head injury should thus arouse the suspicion of the presence of a subdural hygroma.

SPINAL PUNCTURE

Spinal puncture is not diagnostic and cannot differentiate this lesion from that of subdural hematoma. The pressure may be subnormal, normal or increased. The fluid may be clear, xanthochromic or blood-tinged.

In the cases analyzed in Table I, the recorded pressures varied from 6 to 15 mm. of Hg. while the protein content varied from 30 to 180 mgm. per cent.

SUBDURAL PUNCTURE

In this report the group of subdural hygromas occurring in infants is not included. Ingraham and Matson[12] made an excellent study of subdural hematomas and hygromas in infancy and established the diagnostic value of subdural puncture. The technique of the method is fully described in their paper.

ROENTGENOGRAPHY

A fracture may or may not be present and is not necessarily correlated with the severity or size of the subdural effusion. In the cases recorded in Table I, a fracture was present in 15 instances. No predilection for any specific site was conducive to the production of the hygroma. A depressed fracture was noted in two cases.

Pneumoencephalography may be helpful. The most characteristic finding is the absence of subarachnoid filling over one or both hemispheres (Figs. 1 and 2). This blotting out of the subarachnoid patterns was stressed by Abbott, Due and Nosik[1,2,3] in the blast concussion group. In Table I this feature was noted in seven cases.

The presence of subdural air shadows on one or both sides with a fluid level raises a controversial point. Some feel that these shadows are due to a technical error in performance of the encephalogram and merely represent a rent in the arachnoid with passage of air into the subdural space. This probably occurs during vomiting or coughing at the time of the procedure. A normal spinal fluid protein would seem to justify this conclusion, since the emptying of a true subdural hygroma should cause an elevation in the average sample of cerebrospinal fluid, particularly if the subdural collection be xanthochromic or bloodstained.

Others feel that the presence of subdural air shadows represents a true emptying of a subdural hygroma through a rent in the arachnoid that occurred formerly at the moment of injury or at the time of encephalography. These cases should show an improvement following such drainage of the subdural space.

It is the author's practice to verify the presence or absence of a subdural hygroma in these cases by trephining, if symptoms persist following encephalographic drainage.

Ventricular shadows may be small and show little or no displacement in bilateral subdural hygromas. Under such circumstances, ventricular puncture becomes difficult and not without danger, particularly if one attempts to puncture in the premotor area. In unilateral subdural hygromas the roof of the ventricle is depressed on the affected side or the entire body may show displacement away from the side of the lesion. In other cases, the ventricle may appear displaced toward the side of the lesion. Again, in case of doubt, bilateral trephine openings should be made.

SURGICAL TREATMENT AND RESULT

It is now generally agreed that the operative treatment is the simple bilateral trephining of the skull. The opening may be conveniently placed over the frontal, temporal or parietal areas. Because of gravitation of the fluid burr openings placed low in the temporal areas, with patient in the sitting position, would be ideal for maximal drainage.

The dura is not discolored unless an underlying hematoma is present. The dura is frequently found to be tense and when it is opened, a gush of clear, xanthochromic or blood-tinged fluid escapes. The brain attempts to fill the opening but by depression of the cortex with a brain spoon and rotating the head, a considerable quantity of fluid can be obtained. After repeating this procedure several times, the brain falls away from the dura and can be seen to pulsate. Drains (cigarette or rubber tube) are placed beneath the dura and allowed to remain for 24 to 48 hours. Longer periods of drainage offer potentialities of infection and hence should be avoided. Once the drains are in place, fluids are forced by mouth and vein to encourage the cerebrum to regain its former confines.

Other operative procedures have been tried, some of which were puncture of the corpus callosum (Payr, 1916), subtemporal decompression (Naffziger, 1924, Cohen, 1927), "English" decompression (Walsh and Shelden, 1937) and even craniotomy (Haynes, 1944).

The statistics of Table I show that clear subdural fluid was recorded ten times, xanthochromic fluid fourteen times, and blood-tinged fluid but four times. The protein content ranged from 100 to 5000 mgm. per cent. In the group reported by Abbot, Due and Nosik, the protein content averaged 300 mgm. per cent. The amount of fluid obtained may vary from a few cc. to a liter. Cohen[6] recorded 2300 cc. of subdural fluid which was obtained with nine different drainages.

In the review of the cases (Table I) bilateral trephines were recorded in 18 cases while unilateral trephine was recorded in 12.

Three patients died. Twenty-six patients made complete recoveries while three made partial recoveries.

SUMMARY

1. The literature on subdural hygromas has been reviewed.

2. Statistical analysis was conducted in thirty-three cases which were reported in detail.

3. Seven additional cases were contributed to the literature.

4. Symptomatology, diagnosis and roentgenography were discussed.

5. The incidence of subdural hygroma is certainly greater than is recognized and the author urges bilateral trephination in cases which present symptoms as outlined in this report.

6. Bilateral trephination of the skull is the surgical procedure of choice.

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EXPERIMENTS ON HEAD WOUNDING BY HIGH VELOCITY MISSILES*

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MANY of the wounds in modern warfare are produced by steel fragments relatively small in size, which strike the body at high velocities. It has been observed, moreover, that in wounds caused by such missiles the character and extent of tissue damage is often far greater than the size or shape of the missile concerned would suggest. Passage of a small bullet or fragment often brings about an "explosive" effect within tissues and severe injury occurs at considerable distance from the path of the missile. It has become of importance, therefore, to investigate under controlled experimental conditions the mechanism of wound production by high velocity missiles. No attempt will be made at this time to review the literature on the subject, but attention is called to papers by Horsley (1894, 1915)[4,5], Wilson (1921, 1927),[6,7] Black, Burns and Zuckerman (1941)[1] and Callender (1943),[2] and to correspondence in the *British Medical Journal* (1940, July 13 and 27).

The experiments on head injury recorded in this paper have been carried out as a part of an extensive program of research in the Biological Laboratories, Princeton University, on the mechanism of wounding by missiles of high velocity. Other aspects of the research will be reported elsewhere.

The missiles used in the experiments to be discussed were small steel spheres. These were chosen, not alone because of their shape, but also because they could be obtained with a high degree of uniformity in mass and diameter. They have been shot from a specially constructed test gun, the details of which need not be given here. Cats and dogs under nembutal anesthesia have served as experimental animals.

Early in our experiments it became evident that it was of primary importance, not only to examine wounds after they had been made by missiles of known dimensions and masses moving at carefully recorded velocities, but more especially to be able to observe and record as completely as possible the changes as they occur during the passage of a missile through various types of tissues. It is possible to simulate body structures through the use of such transparent substances as water and gelatin gel and to take microsecond flash pictures and also high speed motion pictures (as rapid as 8000 frames per second), which show the changes taking place during and

* The work reported in this paper was done under a contract, recommended by the Committee on Medical Research, between the Office of Scientific Research and Development and Princeton University

immediately after passage of a missile. The tissues of the body, being opaque, are not adaptable to these photographic techniques. However, we have been fortunate in having at our disposal X-ray equipment by which it is possible to take roentgenograms with an exposure time of less than one millionth of a second. This microsecond X-ray apparatus, developed by Ehrke and Slack (1941),[3] consists essentially of a Westinghouse surge generator and a special X-ray tube. Discharge of a bank of condensers in less than a microsecond supplies current of several thousand amperes to the tube. Voltage can be varied from 180 to 360 kilovolts. Using an appropriate trigger device, activated by the passage of a missile, a microsecond roentgenogram can be taken at any desired moment, during or immediately after the passage of a missile through a part of the body. Although the details in these pictures are not so sharply defined as in the conventional roentgenogram, taken with longer exposure time, many important changes in tissues can easily be observed.

One of the most striking and important features in the passage of a high velocity missile through such substances as water and gelatin is the formation of a temporary cavity of large size, compared to the size of the missile. This cavity, at first conical in shape, rapidly expands and, after attaining a maximum size, tends to become spherical and then pulsates several times. In the case of gelatin, a fusiform permanent cavity, which remains after passage of the missile, is far smaller than the temporary cavity observed in high speed motion pictures. In living structures, such as the head, limb and various excised organs of cats and dogs shot with steel spheres, high speed motion pictures (4500 frames per second) indicate that formation of a large temporary cavity, similar to that observed in water and gelatin, takes place. In the case of muscle, for example, an initial large swelling is evident, which pulsates several times. At the end of the pulsation there remains the relatively small permanent wound cavity, to be observed in the later examination of the wound.

Clear demonstration of the presence of a large temporary cavity, which exists only for a matter of microseconds after passage of a high velocity missile, is obtained from microsecond roentgenograms. These roentgenograms show great displacement of tissue about the temporary cavity. In the case of a limb of a cat or a dog, for example, such a temporary cavity within the muscles may result in the fracture of a bone several centimeters away from the path of a missile. Nerves are stretched and small blood vessels often undergo great damage, with consequent extravasation of blood.

We are convinced that the high radial velocity imparted to tissues, as evidenced by the rapidly expanding and pulsating temporary cavity, is a primary factor in wounding. It is especially clear that any evaluation of damage to tissues, not only those directly in the path of a high velocity missile, but also at a distance, must take into account the importance of the temporary cavity.

In the case of head injury resulting from high velocity bullets and fragments, much of the damage to the brain, skull and other structures undoubt-

edly results from pressure developed within the skull as a large temporary cavity is formed in the brain immediately after passage of the missile. The significance of this cavity is demonstrated by the following experiments.

A large dog (weight 52 lbs.) under nembutal anesthesia was shot in the head with an 8/32 inch steel sphere (Exp. 248). The sphere entered the head in the right temporal region and

FIG. 1. Microsecond roentgenogram of the head of an anesthetized dog (Exp. 248), showing a large temporary cavity within the cranium produced by the passage of an 8/32 inch steel sphere. At impact with the head the sphere had a velocity of approximately 4000 feet per second. Entrance of the sphere was at the left in the roentgenogram, exit at the right. For complete explanation see text.

emerged in the same region on the left. The impact velocity of the sphere was approximately 4000 feet per second. Fig. 1 is a microsecond roentgenogram exposed approximately 400 microseconds after impact of the sphere with the head. This roentgenogram was taken from the ventral aspect of the head and the sphere, moving from left to right in the picture, has passed out of the field.

In Fig. 1 the outlines of the large temporary cavity can clearly be seen. This cavity, at the time of exposure, appears to have been approximately 6.5 centimeters in diameter at its widest point. Since our experiments have shown that the cavity grows rapidly in size immediately after passage of the bullet, it is impossible to state whether the cavity shown in this roentgenogram is at its maximum size. However, a comparative study of roentgeno-

grams taken at varying periods after passage of missiles indicates that the cavity shown here is of approximately maximum proportions for the size of sphere and velocity concerned. Examination of the roentgenogram shows great displacement of tissue and extensive fracturing of the skull.

At autopsy, in addition to comminution of the skull at the points of entry and exit of the sphere, severe fracturing was evident throughout the cranium. In particular, there was extensive disarticulation of bones along suture lines, a situation that has been found to be a common occurrence in this "explosive" type of skull damage. The brain stem had virtually been transected

FIG. 2. Skull from the head of an anesthetized cat (Exp. 238) struck in left temporal region by a 4/32 inch steel sphere with an impact velocity of approximately 3800 feet per second.

and cerebral hemispheres and cerebellum were in the condition of a macerated pulp. It is important to emphasize that this widespread destruction had been caused by an 8/32 inch steel sphere.

If internal pressure within the cranial cavity, resulting from the formation of a large temporary cavity, is a primary factor in the extensive skull fracturing and splitting of sutures caused by high velocity missiles, elimination of this pressure should result in marked decrease in the amount of skull damage that occurs. This was tested by the following two experiments.

An anesthetized cat (Exp. 238) was shot in the head by a 4/32 inch steel sphere with an impact velocity of approximately 3800 feet per second. The missile entered the skull in the left temporal region and emerged in the same region on the right.

The results in all respects were similar to those observed for the dog described above. Extensive fracturing of skull bones and disarticulation along sutures occurred. The badly damaged skull of this cat, after being cleaned of soft tissues, is shown in Fig. 2.

A second cat (Exp. 240) was decapitated by disarticulation of the atlas and the occipital condyles. The brain was immediately macerated by means of a probe inserted through the foramen magnum. As much of the brain as possible was then removed through the foramen,

leaving the cranial cavity filled only with air. This head was shot, in the same manner as that described above (Exp. 238), by a 4/32 inch sphere striking the right temporal region with an impact velocity of approximately 3800 feet per second.

The results, shown by the cleaned skull in Fig. 3, are strikingly different from those just described for Exp. 238 (Fig. 2). With the cranial cavity devoid of a brain (Fig. 3) and with an open foramen magnum, the skull damage was relatively minor. Disarticulation of sutures was entirely lacking and only minor fracturing of the temporal bones occurred, restricted to the points

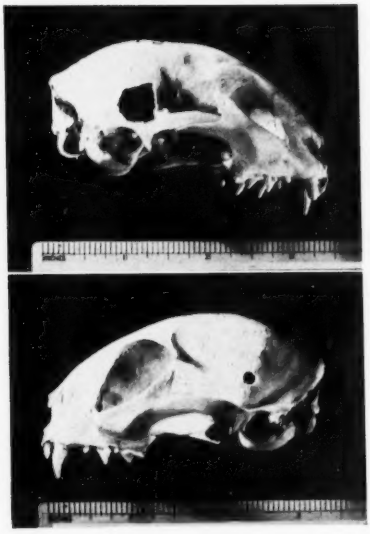

FIG. 3. Skull from the head of a cat (Exp. 240) struck in right temporal region by a 4/32 inch steel sphere with an impact velocity of approximately 3800 feet per second. The head of this cat was severed from the body and the brain removed from the cranium before the shooting. Upper photograph shows entrance of sphere, lower photograph shows exit.

of entrance and exit of the missile. As the sphere entered the empty cranial cavity a stellate fracture of the right temporal bone took place and when the skull was cleaned after autopsy fragments of the temporal bone dropped away, presenting the aspect shown in Fig. 3 (upper photograph). In emerging from the cranial cavity, by penetrating the left temporal bone, the sphere left a neat hole (lower photograph, Fig. 3), with very minor stellate fracturing.

SUMMARY

Experiments demonstrate that a small missile (4/32 to 8/32 inches, diameter) with high velocity (4000 feet per second) in passing through the head of a cat or a dog produces a large temporary cavity within the brain. Pres-

sure within this cavity imparts a high radial velocity to surrounding tissues. A microsecond roentgenogram taken during the shooting of a head clearly shows the outlines of the large temporary cavity. The resulting injury includes extensive disarticulation of bones of the skull along suture lines, compound fractures of individual bones and maceration of the brain. That these injuries are the result of high internal pressure within the cranial cavity, is demonstrated by shooting a cat's head from which the brain has been removed by way of the foramen magnum. Under such circumstances a high velocity missile causes only minor damage to the skull.

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PENETRATING BRAIN WOUNDS. ANALYSIS OF 342 CASES

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COMPLETE analysis of a series of 342 penetrating brain wounds constitutes a difficult and long term task. The patients must be studied over a period of years. The incidence of epilepsy, late infection, psychiatric problems and estimation of the patients' eventual social worth must be evaluated. Such an analysis is beyond the scope of this report, which deals with the actual treatment, postoperative care, and the immediate results. It is desired to stress the repetitious nature of the lesions and to present a resultant classification. The surgical problems encountered, and the methods evolved to cope with them, will be described.

Dr. Cushing's[3,4] series of 133 penetrating brain wounds during the last war, Ascroft's[1] series of 292 such wounds, Cairns'[2] report and the Russian experience[8] have guided our surgical efforts. It was found, however, that some problems had not been solved and that new and more efficient methods had to be found. The burden of neurologic surgery in the field was heavy, and the tedious procedures, familiar to all neurologic surgeons, had to be shortened. It became possible finally to operate upon as many as twelve difficult, penetrating brain wounds in twenty-four hours and still maintain Halsted-Cushing technique. A trained team consisting of instrument nurse, anesthetist, and two medical corpsmen, plus invaluable surgeon-assistants†, constituted the direct solution to the demand for speed and efficiency. Surgical technique and routine must be standardized, despite necessary improvisations.

This series of penetrating brain wounds is collected from the experiences of the author in the North African, Sicilian and Western European campaigns. They are part of a larger experience dealing with the more simple aspects of wartime neurologic surgery, such as compound, depressed skull fractures, scalp lacerations, closed head injuries, spinal cord and peripheral nerve injuries. They were all operated upon by the author, or by an assistant under the author's direct supervision. They were collected from Oran to Tunis, from Licato to Messina, Sicily and from the grim beach-head on Normandy, through France, Belgium, Holland and Germany. They were operated upon, some times under fire, in Clearing Stations, Field Hospitals, and Evacuation Hospitals.

A distorted picture of the magnitude of brain damage caused by war

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TABLE 1

Analysis of 342 penetrating brain wounds

Type of Brain Wound	Disabling Neurologic Sequelae*						Infection					Deaths			
	Number of Patients	Number Operated upon	Blind or Hemianopia	Aphasia	Plegia	Low Mental Content	Scalp	Meningitis	Abscess	Fungus	Osteomyelitis	Preoperative	Postoperative	Over-all Mortality Rate† (percentage)	Postoperative Mortality Rate (percentage)
Small shallow	68	68	0	9	14	0	3	0	0	0	0	0	2	2.9	2.9
Deep narrow	87	78	3	6	19	11	1	2′ ('1 ventriculitis)	16*	8*	0	9	9	20.6	11.5
Orbital or frontal sinus and brain	41	40	14	2	0	2	2	2′ ('1 ventriculitis)	0*	0	0	1	4	12.1	10.0
Base to brain	3	3	0	0	0	0	0	0	0	0	0	0	0	0.0	0.0
Diencephalon (hypothalamus)	13	8	0	0	0	2	1	0	0	0	0	5	3	61.5	37.5
Extensive brain damage	112	92	23	8	26	19	3	3′ ('1 ventriculitis)	2	0	0	20	18	33.9	19.5
Ventricular	(100	77	—included in other categories—									23	26	49.0	33.7)
Cerebellar	5	4	0	0	0	0	0	0	0	0	0	1	0	20.0	0.0
Midbrain	13	3	0	0	0	0	0	0	0	0	0	10	2	92.3	66.6
Total	342	296	40	25	59	34	10	7	18	8	0	46	38	24.5	12.8

* Of those patients surviving, 42 per cent are normal, socially acceptable and useful individuals. The 16 abscesses and 8 fungi were present on arrival. Only 2 abscesses and no fungi were seen in the Western European campaign.

† All patients reaching author alive.

wounds is seen if this series is accepted casually. A disproportionate number of patients suffering extensive brain damage has been included in this analysis. Most of these patients with extensive brain damage, or presenting technical difficulties, were seen and operated upon in consultation. The mortality figures are inaccurate for the same reason, although they represent the true mortality of severely damaged brains. Minor brain wounds do not constitute a large part of this series. No wound that did not penetrate into the brain is included.

Small pieces of shell casing caused a tiny hole of entrance through the skull. A deep, narrow, missile tract reflects a relatively minor amount of concomitant diffuse brain damage.

Larger pieces of shell fragment, or rifle and machine gun bullets, caused much more brain damage at the point of entry. The tract assumed an explosive pattern at the exit wound or at the cessation of forward progress. Extensive maceration, softening and hemorrhage marked this area of the brain.

Gutter wounds of the brain caused the most disastrous type of brain damage. This was caused by a large fragment striking the skull and driving fragmented bone, and the large metallic foreign body, through the brain and out again. Much indriven bone and macerated brain was left behind. This was seen commonly in the frontal and occipital lobes, because of the prone position of the soldier. It was the prime reason for the inordinate number of "lobectomy necessitans" performed.

Almost all the brains of the patients who died pre- and postoperatively were examined at necropsy. The wave of force accompanying the missile caused both local and remote petechial hemorrhages. This force was particularly marked in gutter wounds and petechial hemorrhages were numerous throughout both the white and grey matter. Pontine hemorrhages and contrecoup hemorrhages were common, but the most spectacular occasional finding was the distribution of areas of hemorrhage and softening to follow the wave of force. For example, a severe occipital gutter type of brain damage revealed, at necropsy, severe local brain damage manifested by softening and hemorrhage, a pontine hemorrhage, and then evenly distributed areas of marked petechial hemorrhages, evenly alternated with areas of normal brain. These would extend in a posterior-anterior direction and the tip of the frontal lobe might be spared, to indicate that it was a sine wave of force rather than a contrecoup phenomenon.

OPERATIVE PROCEDURES

Preoperative Care and Selection. The care of the patients in this period is all important. Many are conscious and alert, and these present no problem. Most of the patients suffering extensive brain damage were in coma of varying depths, with either a thin, thready, rapid pulse and stertorous, rapid respiration or with a slow, bounding pulse and Cheyne-Stokes type of respiration. Thus they presented either the picture of cerebral insult (cerebral decompensation or cerebral shock) or increasing intracranial pressure. The latter condition was, by far, the more rare.

It was found that these patients need shock treatment and a period of stabilization as urgently as one in true shock due to blood loss. The same measures were instituted: prone position, oxygen, aspiration of the respiratory tree if moist, plasma, whole blood, and caffeine to promote adequate cerebral circulation and diuresis. Despite the fact that the cerebral insult was not due to blood loss, it was found that whole blood in quantities gave the most dramatic results. A patient considered to be dying a central death, by the use of whole blood could be roused to the point where surgery could be accomplished and a life saved. Plasma was a useful adjunct but nothing

could equal the efficiency of whole blood in the stabilization of vital signs.

Just as an abdominal wound or a fractured femur, a brain wound reaches a peak, an optimal level, when surgery must be performed. Rarely may a secondary peak in vital signs be reached if surgery is delayed and the vital signs again fail. Usually death is the result if the peak of preoperative condition is reached and ignored.

X-rays are taken only after the vital signs stabilize. Excessive manipulation, such as shaving the head or positioning on the x-ray table, is avoided. Paraldehyde is the drug of choice to control restlessness. Fluids are maintained to basal requirements and penicillin and sulfadiazine therapy started.

Patients responding more slowly, or obviously dying, were left for further stabilization. They were usually given the chance of surgery if they did not respond to such measures and still appeared moribund after several hours of treatment. A small proportion of these patients were saved by surgery in the face of apparently irreversible damage.

War-time neurologic surgery is seldom life saving. That it may be is due to relief of medullary compression, intracerebral or intraventricular clots, subdural and epidural hematomas and foreign bodies in areas incompatible with life. It is usually surgery to prevent later infections, epilepsy or further loss of functional brain tissue. Therefore, a period of waiting for stabilization can be prolonged to even 48 or 72 hours if it is thought it will help the patient over the hurdle of the operation.

Operative Technique. Actual surgical technique, necessary for the successful treatment of penetrating brain wounds, has already been outlined.[3,4,7] Adequate resection of devitalized brain tissue to healthy margins, removal of fragmented indriven bone, hemostasis and primary complete closure in layers are established routine. Sulfanilamide or penicillin powder, or both, were instilled in every missile tract. Lighted brain retractors could be used in large brain defects, but in smaller missile tracts they were found impractical. A suitable brain needle was found to be invaluable and, in the author's hand, replaced Cushing's small rubber catheter. The brain needle acted as an extension of the operator's finger, little tactile sense being lost. Narrow missile tracts could be followed with ease, bone fragments and foreign bodies localized, macerated brain and blood clot aspirated, irrigation accomplished and penicillin solution instilled. The dura mater was always closed tightly. Grafts were obtained, whenever necessary, from adjacent pericranium, temporal fascia or fascia lata.

Anesthesia. It was felt in the beginning that local anesthesia, supplemented by sedation, would be sufficient. It was soon realized, however, that the number of cases required rapidity of surgery, and the restlessness and apprehension of the patient made a more complete anesthesia desirable. Accordingly, sodium pentathol, in a $2\frac{1}{2}$ per cent solution, was used to induce the patient and to allow painless infiltration of the scalp with 1 per cent novocaine solution to which epinephrine had been added. The patient was

carried in a very light plane of anesthesia, so that he would stir if non-anesthetized scalp was grasped. This allowed the local anesthetic agent to carry the burden of anesthesia, and the pentathol merely served the purpose of inducing sleep, amnesia, and lack of apprehension. It did not depress vital medullary centers and all in all constituted one of the most successful anesthetic combinations.

Types of Wounds. Depressed skull fractures are not included in this series. It is startling, however, to find that in the majority of those instances there is, under an intact dura, a subdural hematoma and a shallow area of brain maceration. This finding has been almost constant, and was at variance with previous conceptions of depressed skull fractures in the acute stage. Those wounds causing brain maceration are included here. Consequently, the dura is now opened in all such cases and the brain wound treated according to the above principles.

Small, shallow penetrating brain wounds were treated by the usual method of resection of non-viable brain tissue, removal of fragmented bone and foreign bodies if accessible, instillation of penicillin and sulfanilamide, and complete primary closure.

Deep, narrow missile tracts were treated with the brain needle as described above. These may on occasion pass through the base of the skull from the face, or from the suboccipital region, into the brain. It is technically impossible to clean out these missile tracts by any orthodox approach, but it was found that they could be adequately cared for by the use of a brain needle threaded through the bone defect into the brain. A unique approach was used when the missile lay superficially, just under the cortex. A cortical incision was made through a burr hole, unless the motor strip or vital speech areas were involved. The foreign body was found, removed, and through-and-through irrigation carried out to properly cleanse the path of the missile and the ventricle. This relatively minor procedure gave good results (Figs. 1 and 2).

Orbital, or frontal sinus injury associated with brain damage, constituted a problem. It was found, however, that it was rarely necessary to turn a frontal bone flap to repair this damage. It could almost invariably be accomplished through the original traumatic defect (Fig. 3). All of these patients received a dural graft and it was unnecessary to pack any one of them. There were many instances wherein an eye was destroyed and the missile had passed into the cranial cavity. Frontal lobe maceration due to posterior orbital plate fragmentation was commonly seen. An eyebrow incision through periosteum, to allow gentle retraction of orbital contents forward, afforded ample exposure to repair the brain wound. It was found that a maxim could be established as to penetration or non-penetration into the cranial cavity. Visualization of the optic foramen and superior orbital fissure, below an intact orbital plate, allowed one to state that the cranial cavity had not been entered by a missile. This is true because of the posterior inclination of the floor of the anterior fossa. The floor of the orbit, below the

optic foramen, comprises the roof of the antrum. This rule of thumb was of great value in combined orbital and intracranial wounds.

Hypothalamic, and midbrain wounds were treated by use of the brain needle so that as little damage as possible was caused to these vital centers.

Cerebellar lesions were very rare, probably due to the proximity of medullary vital centers. It was possible to operate upon only four of these patients, and the same principles described above were followed (Fig. 4).

Extensive brain damage, usually caused by gutter wounds of the skull and brain, constitute a large part of this series.[6] These patients were gravely wounded and appeared *in extremis* upon arrival at the hospital. They were in coma, and macerated brain tissue was extruding from the large skull defect. These are the instances that were responsible for the virtual "lobectomy necessitans." This term means only that the traumatic amputation of one or more cerebral lobes was completed. The maceration of brain tissue was extreme, caused not only by large indriven bone fragments but also by the shattering force of the missile. Lobectomies were completed by means of suction and irrigation. All devitalized brain was removed (Fig. 5).

Trans- or intraventricular brain wounds constitute a problem not easily solved.[5] It was noted that these patients rapidly deteriorated and that the prognosis was poor. It was necessary to follow the missile tracts to and through the ventricle. Hemostasis must be absolute. Irrigation of the ventricle was necessary to remove blood clots and macerated brain or ependyma. This procedure must be complete and careful because of the danger of hydrocephalus and death if the foramen of Monro is occluded, if the ventricular system has filled with blood clot, or if bleeding is allowed to persist. Penicillin solution was then instilled directly into the ventricle. Intraventricular foreign bodies, unless easily accessible, were left *in situ* until the ventricle dilated and the removal was thereby facilitated.

Postoperative Care. A patient undergoing the cerebral insult consequent to a penetrating brain wound and the resultant surgical repair, requires detailed, careful, postoperative care. These patients are segregated into a neurosurgical ward where a trained nursing and enlisted personnel may observe and care for them. Suction and oxygen must be available at all times. The head of the patient's bed is elevated, to promote cerebral venous drainage. Caffeine is given in small doses to increase cerebral circulation and promote diuresis. Fluids and whole blood are administered freely, with no regard to restriction of fluids below 3,000 cc. per day. A Levine tube is passed so that food and fluid may be furnished easily to the patient. He is turned frequently to reduce the incidence of hypostasis. Sulfadiazine is given by mouth or by the intravenous route. Penicillin is given intramuscularly for 72 hours to prevent soft tissue infection which may lead to an infection of the central nervous system.[2] Intrathecal penicillin is used when infection is threatened or is already present. Paraldehyde, 4 cc. intramuscularly, is the drug of choice for restlessness and sedation. Once any local pressure has been removed from the cranial cavity, the judicious and

cautious use of repeated lumbar punctures, to reduce generalized cerebral edema, is recommended. Osmotherapy, such as the administration of hypertonic glucose or sucrose, has not been used. Hypertonic proteins, such as plasma, seem to show promise.

USE OF PENICILLIN AND SULFANILAMIDE, AND INCIDENCE OF INFECTION

Sulfanilamide powder was used locally on all brain wounds in the first 161 cases. It was the drug of choice because of the reported danger of convulsions when sulfathiazole or sulfadiazine is used. Extensive oral or intravenous sulfadiazine therapy was carried out on all patients with brain wounds.

TABLE 2*

Comparative incidence of infection with use of sulfanilamide powder and combined sulfanilamide-penicillin powder

Local Use of	24 Hours		48 Hours		72 Hours		96 Hours		Over 96 Hours	
	Patients	Infection	Patients	Infection	Patients	Infection	Patients	Infection	Patients	Infection
Sulfanilamide powder	84	0	26	2	18	6	6	2	27	24
Combined sulfanilamide-penicillin powder (5 gm. to 40,000 Oxford units)	121	1	12	3	18	3	6	3	4	1
Combined Total	205	1	38	5	36	9	12	5	31	25

Infection incidence over-all — Sulfanilamide 21.1% — Sulfanilamide-Penicillin 6.8% — Over-all this series 13.9%

* This table covers only a ten-day observation period. The delay in evacuation, in the penicillin series, was at Falais Gap, where wounded Germans lay in muddy fields for days before they could be reached. Many factors enter into this computation. Delay in reaching the surgeon and adequacy of surgery are of vital importance and may be of more value than either drug. This contrasting series is not conclusive as to comparative value of the two drugs.

Later, during the invasion of France, penicillin became available. Reluctant to decide that wounded Americans could not have the advantage of either or both drugs, merely for the sake of a contrasting series, the author used a combination of 40,000 units penicillin in 5 gm. of sulfanilamide powder in the next 161 cases. Parenteral (intramuscular) penicillin and oral or intravenous sulfadiazine were used routinely, postoperatively, in all cases after the first 62.

Intraventricular penicillin solution (20,000 units) was used in all ventricular wounds and was followed by intrathecal penicillin every day (40,000 units). Deep, narrow missile tracts were treated by instillation of 20,000 units in solution into the tract.

The result of the above treatment is seen in Table 2. It should be remembered that the bacterial flora of Europe is more virulent than that of Africa and Sicily. At Falais Gap, when the German 7th Army was cut off and annihilated, German patients were received with extruding macerated brain tissue, having lain for 4 and 5 days in a muddy field. These conditions distort the picture, but the author concluded that penicillin and sulfanilamide powder are of greater value in preventing cerebral infection than sulfanilamide alone.

The most striking results were seen in ventricular wounds treated by prophylactic instillation of penicillin into the ventricle followed by penicillin intrathecally. No patient who developed ventriculitis survived, but the author feels that many cases of ventriculitis were so prevented. Patients with meningitis secondary to penetrating brain wounds were cured by the intrathecal use of penicillin. Deep, narrow missile tracts, particularly prone to infection, rarely became infected when liquid penicillin was instilled into their depth.

Adequate surgery cannot be replaced by drugs. Non-viable brain tissue must be resected to healthy margins, but to conclude, because of a lower incidence of infection and a lower mortality rate, that our technique is superior to that of the master surgeon, Cushing, is stupid.

The author concluded that penicillin was a drug that was non-irritant to brain tissue and primarily non-convulsive. He ascribes the great reduction in cerebral infection in this war to rapid evacuation of brain wounds to the neurologic surgeon, prophylactic local use of penicillin and sulfonamides and therapeutic parenteral and intrathecal use of penicillin.

PROGNOSIS AS ALTERED BY TYPE AND LOCATION OF BRAIN WOUND

It was repeatedly observed that wounds involving certain areas and structures of the brain allowed one to prognosticate as to life and that they followed a fairly clear-cut course depending upon the area damaged.

Patients with penetrating small arms or small shell fragment wounds through silent areas, if they survived to reach the neurologic surgeon, lived and did well.

Frontal lobe damage, and frontal lobectomies, unless the damage extended to the precentral gyrus, offered an excellent prognosis as to life, and even, grossly, as to future social worth. Frontal lobectomies, because of extreme maceration of brain tissue, were common. The loss of one frontal lobe did not seem to grossly affect the patient's higher psychic faculties. Not uncommonly, the tip of the opposite frontal lobe was resected as well. Even this apparent gross damage was well hidden under a normal social behavior. Some inhibitions were lost, on occasion, but the defect was not incapacitating. Complete bilateral loss of the frontal lobes, however, reduced the individual to a vegetative state.

Extensive occipital lobe damage did not share this favorable outlook. This may have been due to the proximity of the midbrain and the wave of

force reaching vital centers. On two occasions, swift resection of a macerated occipital lobe and evacuation of a large intracerebral hemorrhage, proved life saving. This was probably due to relief of pressure, exerted through the incisura of the tentorium, upon the brain stem. On the whole, however, extensive occipital damage carried a poor prognosis. The neurologic defect exhibited by such a patient, if he survived, was only that of a homonymous hemianopsia, unless the diffuse brain damage interfered with other functional areas.

The prognosis of *parietal and temporal lobe wounds* seemed to be dependent upon further penetration of the missile into the diencephalon, hypothalamus or ventricle. The neurologic deficit after such wounds was lamentable; paralysis, aphasia, alexia and agnosia, depending upon the area involved, were common.

Diencephalic penetration (*hypothalamus and third ventricle*), even if the missile was small, carried a poor prognosis. Autonomic functions and heat regulation were so disbalanced as to cause death in most cases.

Mesencephalic lesions offered a poor prognosis, and in only one instance was it possible to remove a large foreign body from the vicinity of the midbrain, at the level of the quadrigeminal plate, and have the patient live (Fig. 6). The remainder of the midbrain lesions did poorly.

Brain stem, pons and medullary lesions were not seen, because of probable instant death on the battlefield.

Cerebellar lesions were very rare because the damage usually extended to the vital centers. Only four cerebellar wounds were operated upon. The lateral hemisphere only was damaged in all four instances. All four patients recovered.

Laceration or destruction of the large venous sinuses of the brain, while causing some technical difficulties, did not necessarily cause death nor did the prediction of spastic quadriplegia come to pass. The author, many times, passed through, caused, or observed, thrombosis of the sagittal sinus in its anterior $\frac{2}{3}$. The lateral sinus was frequently involved and the junction of the sagittal and transverse sinuses, the torcular, was blown away not infrequently. The posterior $\frac{1}{3}$ of the sagittal sinus was involved in three cases and, after thrombosis, caused no gross neurologic defect.

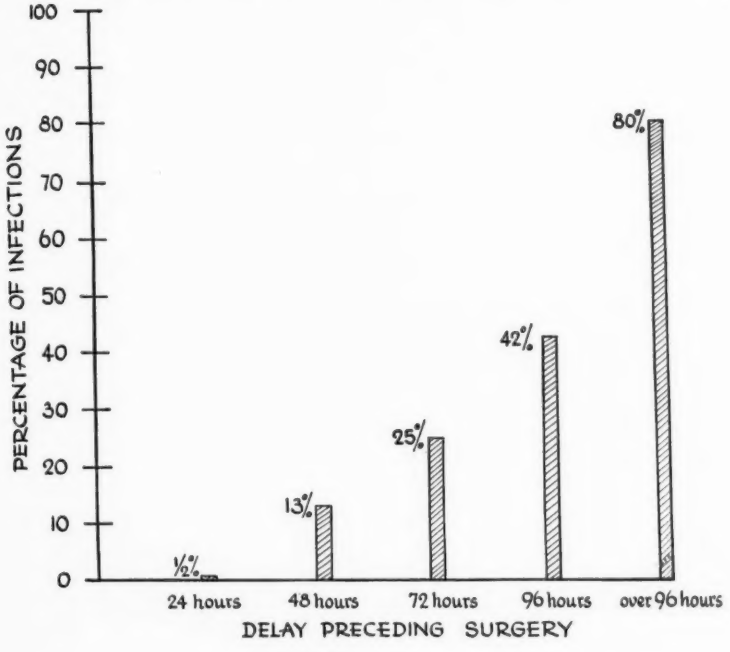
Ventricular wounds constituted a grave problem. A small missile tract passing through a ventricle was likely to cause death. Extensive maceration of the ependyma, or the existence of a large blood clot in a ventricle, seemed incompatible with life. The foramen of Monro was occluded by clot and debris in some instances. The resultant unilateral hydrocephalus, seen at necropsy, was judged to be the cause of death. It was found that patients with moderately large ventricular wounds could be saved if the ventricle could be completely cleansed of debris and clot, and if intraventricular bleeding could be stopped. This was done by means of suction and irrigation, not always under direct vision.

Another type of cerebral wound causing an unfavorable prognosis is that

in which a missile passes through the *orbit or frontal sinus* and travels back to either the parietal or occipital lobes. The author attributes this to its transventricular passage and to the technical difficulties involved in properly cleaning out the missile tract.

Three patients exhibited a combined extensive penetrating brain wound and a spinal cord wound. The result seemed satisfactory in one instance. The left frontal lobe, tip of the right frontal lobe, right frontal sinus and right eye were destroyed. His spinal cord lesion was incomplete and laminectomy allowed complete recovery of function. His mental status when discharged was good. He was a socially acceptable individual. One other patient had an incompletely transected dorsal spinal cord, although he recovered from his severe brain wound. The other patient died of a severe transventricular brain wound. His cord had been transected.

CHART 1. *Incidence of infection as determined by delay in reaching the neurologic surgeon*



MORTALITY

The mortality and infection rate of brain wounds has been more than halved since the last war. It has been materially reduced since the beginning of this war. A smaller series might portray a lower or higher mortality rate. This series is thought to be of sufficient size to allow for variations.

An attempt can be made to place brain wounds in their proper relation to other severe war wounds. Over-all mortality of all wounds reaching a front line hospital was roughly 3 per cent. That of penetrating abdominal wounds was 21 per cent and that of all compound fractures reaching a front line hospital was 5 per cent. Thus, an operative mortality of 13 per cent for penetrating brain wounds seems encouraging.

The actual figures of the postoperative mortality are given in Table 1. Any estimation of mortality is prone to distortion because of many factors. Distance from the front lines is an important element. Severely wounded patients, who survive arduous transportation some distance to the neurosurgeon, stand reparative surgery well. The surgeon very near the front, however, will see and operate upon gravely wounded soldiers who would never reach alive an installation farther back. He will also save a certain percentage of patients who would otherwise be lost. He will prevent postoperative infection (Chart 1), but his mortality rate will rise. Thus with this series. It was felt that certain patients, apparently moribund, could be saved if surgery was resorted to. Some were inevitably lost, others saved.

SUMMARY

1. Analysis of a series of 342 penetrating brain wounds is reported.

2. Brain wounds are classified as to type, location, pathologic and surgical peculiarities.

3. Prognosis, as dependent upon type and location of wound, is attempted.

4. Technical details of surgical repair are described.

5. Infection and mortality rates are arrived at.

6. Credit for lowering of both is given to swift evacuation to neurologic surgeons; early, primary, definitive surgery; and the use of penicillin and sulfonamides.

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TYPICAL X-RAYS OF PENETRATING BRAIN WOUNDS

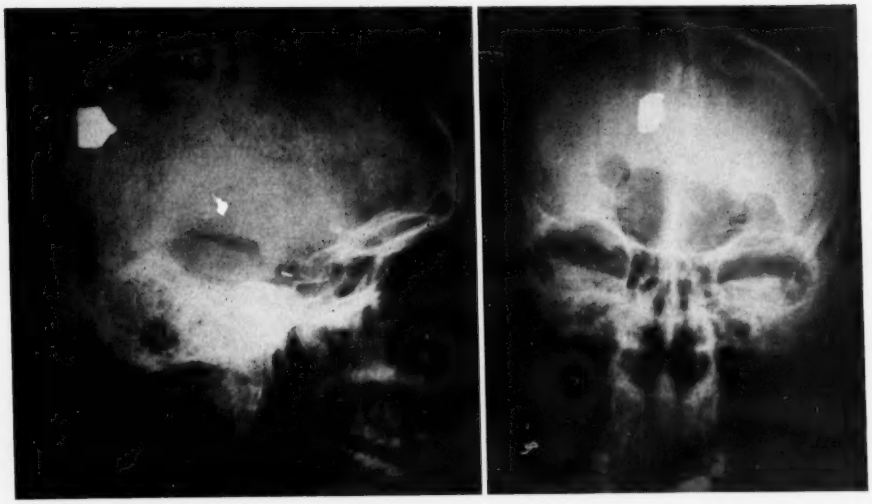

FIG. 1.

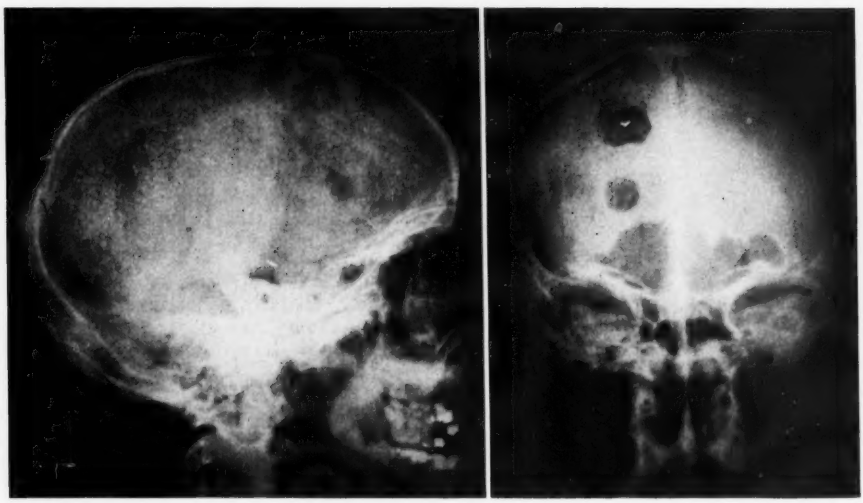

FIG. 2. Postoperative x-rays in case shown in Fig. 1.

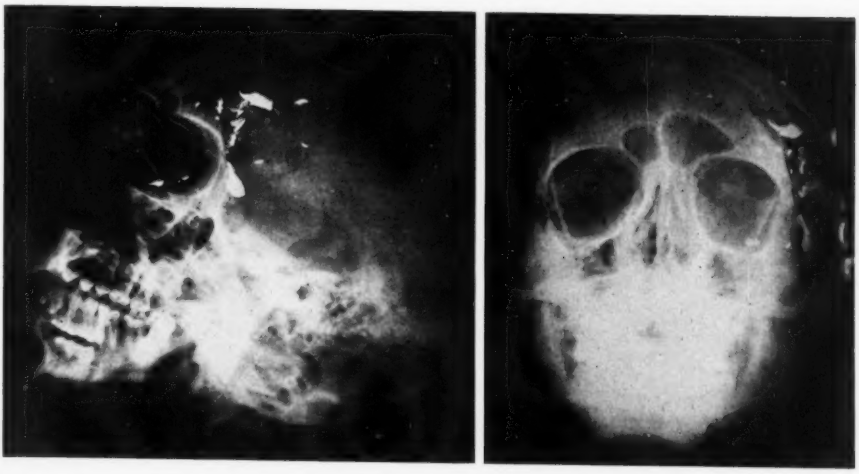

FIG. 3.

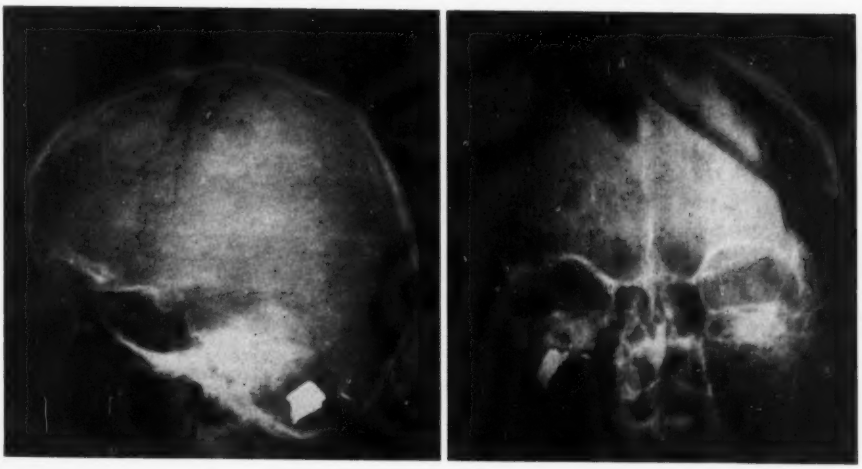

FIG. 4.

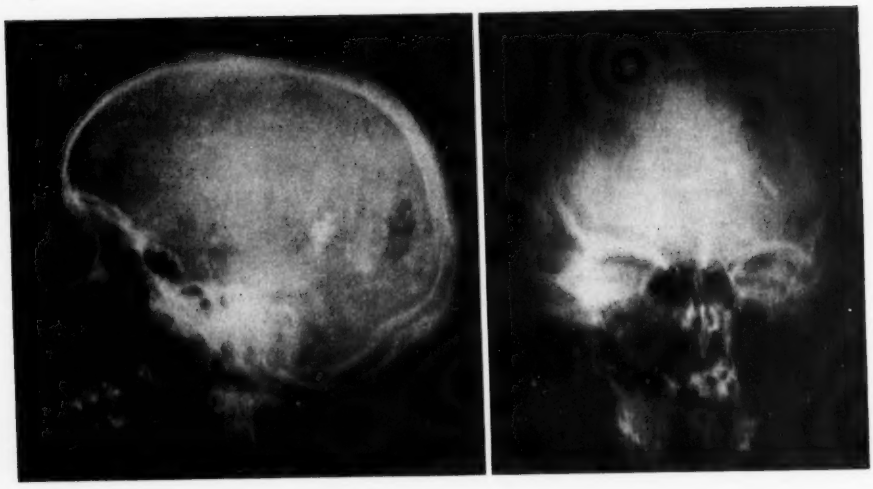

FIG. 5.

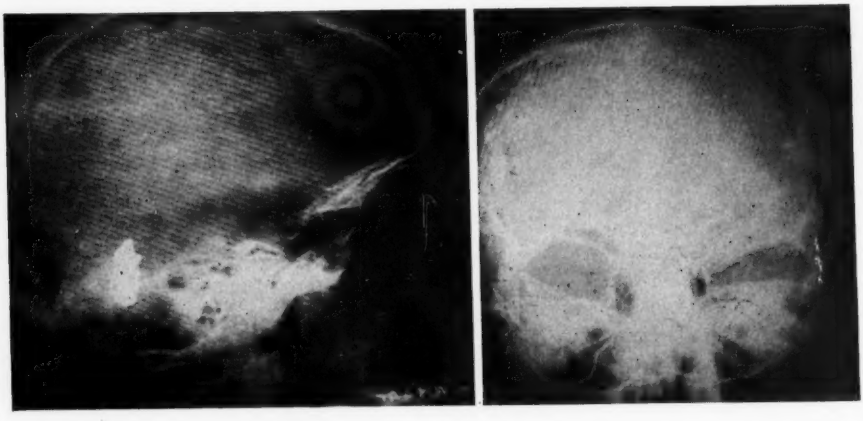

FIG. 6.

THE REDUCTION OF HERNIA CEREBRI BY TANTALUM CRANIOPLASTY

A PRELIMINARY REPORT

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HERNIA CEREBRI or fungus cerebri, as the terms have been used synonymically, has long been an enigma of the neurosurgeon. In military practice this distressing complication occurs with such frequency as to constitute a major surgical problem.

While it is not the purpose of this report to discuss all the factors considered to be operative in the production and evolution of this condition, it is well to describe the general nature of battle-inflicted cranio-cerebral injuries and to point out those factors that are generally held to be conducive to the formation of hernia cerebri.

Typically such wounds result from the impact upon and/or penetration of the cranium by high velocity missiles of small mass. The scalp itself may be lacerated or avulsed in any conceivable manner. Fragmentation of the inner and, to a lesser extent, of the outer tables of the skull ensue, the fragments of bone being showered along the projectile path. Considerable portions of the skull may be avulsed in this process and the dura may be disrupted, lacerated or devitalized for distances well beyond the margin of the skull fragmentation. Radial linear fractures usually extend from the area of central fragmentation and occasionally remaining large fragments of skull are left in positions of extreme elevation or depression.

Insinuated into the pulpified cerebral tissue are, from within outward, the metallic foreign bodies, a trail of bone chips, pieces of scalp and hair, fragments of the helmet liner, such as wool threads and fiber, and frequently splinters of the helmet itself. Consequently such wounds are always contaminated if not actually infected. This fact establishes the first condition favorable to the formation of herniation of the brain.

The second factor that may contribute to the formation of brain herniation is failure to attain the criteria of thorough operation. By thorough operation, as officially delineated in this theatre, is meant the removal of all technically and anatomically accessible foreign bodies and bone chips, removal of pulpified cerebral tissue in the wound tract, repair of the dura by primary suture or any effective method of grafting, and suture of the scalp without drainage by any surgically sound manoeuvre.

Thirdly we are confronted by the consideration of intracranial hypertension. In warfare surgical treatment may be administered in a matter of hours or days, depending upon the fortunes of battle. Regardless of time, however, it may be postulated that at some stage cerebral edema will ensue in such wounds with or without operation. The result is of course an increase

of intracranial tension or intracranial mass, which situation logically favors herniation.

Fourthly, any combination of infection, cranial defect, or intracranial hypertension may produce disturbances of vascular cerebral circulation or of the cerebrospinal hydrodynamics. The resultant distortion of the brain may produce ischemic necrosis and may prevent chemotherapeutic agents from reaching the pathological area. In addition, this condition contributes to interstitial edema and thereby to intracranial hypertension.

A fifth closely related factor may be of importance in war wounds. These patients have frequently experienced severe hemorrhage, lengthy periods without food, and energetic efforts at replacement therapy with plasma, blood, and other infusions, all of which alter the osmotic characteristics of the circulating blood.

These then, briefly, are some of the factors that set the stage for the advent of cerebral herniation. Further contemplation of the situation merely gives one the impression that all these factors may become interacting in a vicious cycle of pathophysiological catalyticism.

The conventional mode of treatment of such lesions, as outlined by the experiences of Cushing in the last war, centered about simple and logical principles, namely,the protection of the hernia from irritation by constant soft dressings, resection of the necrotic portions, control of infection, and the reduction of intracranial tension by dehydration and repeated spinal drainages. The statistical results of this treatment are well known. Not infrequently the hernia was not controlled, but rather, herniation was progressive, attended by a corresponding neurophysiological loss. Finally the dreaded sequelae of spontaneous ventriculostomy, ependymitis and death were ever impending.

The mechanical restraint and subsequent reduction of hernia cerebri, which represents a departure from the foregoing conservative therapy, will be described and illustrated by six brief case reports.

Case 1. A 27-year-old infantryman was admitted 8 August 1944. He had been wounded by artillery 12 days previously and had had primary debridement the day of wounding in a forward hospital. The patient was lethargic and complained of headache and blurred vision. There was suggestive weakness of the left lower leg, though cooperation was poor. The optic discs showed early immeasurable blurring. Blood studies were within normal limits. The temperature curve was a few tenths below normal. Radiologic recheck revealed a right postparietal craniectomy 4×5 cm. Five cm. deep to this defect was a solitary bone fragment ½×1×2 cm. The wound was grossly bulging, and yellowish fluid was exuding from a small aperture in the middle of the incision.

Operation: 9 August 1944. The old wound was reentered. Yellowish necrotic cortex presented beneath. In removing the fungating mass a tract was uncovered from which viscous yellow pus escaped. The abscess was readily evacuated and the bone fragment recovered from the cavity. There was still a disturbing tendency for the brain to continue extrusion. The dura was not repaired. Wishing to restrain the brain from further extrusion, even if only temporarily, a tantalum cranioplasty was carried out, the plate being furnished with a central drill hole through which a latex tube was inserted into the depths of the abscess cavity and brought out through a central stab wound of the scalp. The remainder of the incision was

sutured tightly in one layer. A waiting suture was placed through the stab wound. The drain was subsequently removed at the rate of 1 cm. every other day.

Result. At the 15th postoperative day the wound was healed. The patient was alert, free of headache, and ambulatory. The optic discs were normal. He was transferred on the 21st postoperative day.

Case 2. On 8 August 1944 a 24-year-old infantryman was admitted who had sustained a left midfrontal penetrating wound of the cranium 8 days previously, which had been debrided the same day in a forward hospital. The patient had weakness of the right lower extremity, had some difficulty in speaking, and complained of headache and stiff neck. Radiologic recheck revealed three sizable bone fragments about 5 cm. deep to a 3×4 cm. craniectomy. The linear operative wound had broken down and necrotic cerebrum was extruding.

Operation. On opening the wound the day of admission the brain was seen to herniate 2 cm. above the skull level. On looping off the extruding portion a considerable quantity of pulpified brain escaped from the missile tract. The bone fragments were removed. The dura was repaired by fascia lata graft and tantalum cranioplasty was carried out.

Result. This patient was transferred on his 8th postoperative day. Follow up three weeks later revealed that the wound had healed primarily, speech was normal, headaches had subsided and he was ambulatory.

Case 3. On 12 August 1944 a paratrooper was admitted who had been wounded by mortar fire 20 days previously. The wound had been primarily debrided at a forward hospital the day of injury. This patient complained of headaches, exhibited spastic paraparesis and was quite unreliable in the management of his urination. He was not mentally clear. Radiologic recheck revealed a right parasagittal craniectomy near the vertex measuring 4×5 cm., below which there were two bone chips about 1½ cm. in diameter lying at a depth of 3 cm. The scalp was intact and healed, though tense, bulging and non-pulsating.

Operation: 13 August 1944. The wound was reentered. No dura was in evidence. After evacuation of a subgaleal hematoma, the denuded cortex presented, bulging to a level of 1½ cm. above the skull. The sagittal sinus was visible in the wound. A rather clean missile tract was seen, through which the bone fragments were removed. The presenting large cortical veins were compressed at the skull margins, and engorged distally. Graft repair of the dura could not be technically done without endangering the sinus, so the cortex was overlaid with fibrin foam and cranioplasty carried out in the usual manner. Closure was tight in layers without drainage.

Result. This patient was transferred 18 days postoperatively, at which time his spasticity had disappeared and his headaches had subsided. He was mentally clear and urologically competent.

The following three cases illustrating this method of hernia cerebri management have been generously contributed by Major Wesley A. Gustafson, M.C., A.U.S.

Case 4. A 30-year-old male was wounded in the right parietal area on 11 October 1944 by high explosive. He received primary debridement the same day, at which time the scalp was closed in one layer. He was admitted to Major Gustafson's service on 28 October; the wound was disrupted and a hernia, 7×10 cm. with 2½ cm. elevation, presented. Culture revealed anaerogenic colon bacillus. He received daily spinal puncture drainages from 28 October until 13 November together with appropriate chemotherapy. The cerebrospinal fluid pressure remained steady at 200 mm. Hg. The herniation was not reduced by this treatment. On 20 November the patient developed meningitis, the same organism being cultured from the cerebrospinal fluid. This was treated by urea and sulphadiazine. The patient became afebrile on 22 December.

Operation: 22 December 1944. The hernia now measured 10×12½ cm. with 2½ cm. eleva-

tion. Cranioplasty was carried out and the hernia manually reduced and held in place by the plate. The dura was not repaired.

Result. The wound was healed by primary intention by the 9th postoperative day and on 18 January 1945 the patient was ambulatory and devoid of headache.

Case 5. A soldier 23 years of age sustained a right parietal penetrating wound on 7 October 1944 by an unknown missile. The wound was primarily debrided on 8 October 1944 and the dura was closed. He was received by Major Gustafson on 24 October 1944 with the wound disrupted and a hernia 5 ×4 cm. presenting. The elevation was 2½ cm. The surface was grossly contaminated. He received daily lumbar punctures for six days, the intraspinal pressure averaging 200 mm. Hg. He was unimproved. The wound was then treated locally with azochloramid and acetic acid solution.

Operation: 26 December 1944. Dural repair by periosteal graft and tantalum cranioplasty.

Result. Postoperatively he was treated by spinal puncture drainages for five days. On 18 January 1945 the patient was up and around and the only neurological residual exhibited was loss of position sense in the left hand. He had no subjective complaints.

Case 6. A soldier 19 years old sustained a penetrating left parietotemporal wound on 6 December 1944. He received primary debridement the day of wounding, but persistent oozing required the placing of 4 vaseline packs in the wound. On 10 December this patient suffered four generalized convulsions. He was admitted to the service of Major Gustafson on 13 December 1944 with the wound disrupted and a hernia, measuring 6 ×2½ cm., presenting. The elevation was 2 cm. He was treated conservatively by daily spinal puncture drainages for 7 days without notable improvement.

Operation: 26 December 1944. Tantalum cranioplasty was carried out without attempting to close the dura.

Result. He was treated for 5 postoperative days by lumbar spinal drainages; culture of fluid from the first drainage yielded streptococci. The sutures were removed on the 8th postoperative day after primary healing. On 18 January 1945 the patient was well, had no complaints and exhibited only slight residual aphasia.

TECHNIC

In most instances it was found that the prolapsing sector of the brain was intimately associated with the meninges by pan-arachnoiditis. These adhesions were gently separated by cottonoid strips or dental roll dissectors. Very often it was necessary to remove the necrotic portions of the hernia by electrosurgery. However, only the devitalized portions were resected. The consequent bleeding was controlled in the usual manner or by fibrin foam. Where possible the dura was repaired by pericranial or fascia lata graft. In the presence of gross infection the dura was not repaired. After the skull edges had been inlaid by chisel, the inlay usually measuring about 3 or 4 mm. in depth and width, the brain was manually depressed by use of a brain spatula and the plate secured in place. Very little force was necessary to recontain the prolapsing portion within the cranial vault.

In the first three cases the plates were secured by drill holes and three steel wires. In the latter three cases the plates were secured by wedging, much in the same manner as a picture-frame back is secured. In all instances, excepting the case of brain abscess, the closure was tight without drainage. It should be noted that frequently the scalp requires aspirating after cranioplasty, particularly if the dura is left unrepaired.

CONJUNCTIVE THERAPY

No doubt this procedure would be impossible without the aid of modern chemotherapy. All these patients were prepared for operation by the use of azochloramid locally when the wound was disrupted or infection evident. For variable periods, both pre- and postoperatively, these patients received both penicillin and sulphadiazine. Penicillin was given in doses of 20,000 units intramuscularly every four hours. Those patients with meningitis, brain abscess or grossly infected hernia were given penicillin intrathecally in doses of from 20–40,000 units once or twice daily.

Intracranial pressure was combatted in two of the first three cases by restriction of fluids and the use of daily infusions of human serum albumin. In the latter three cases fluid restriction was supplemented by spinal puncture drainages.

RATIONALE

This procedure restores the herniating cerebrum to the cranial vault and corrects the internal contours of the skull to their normal state. In so doing it obviates the marginal compression of the cerebral vascular channels and perivascular spaces, thus relieving hyperemia or ischemia as the case may be. Further, repeated contamination and mixed infections are avoided by tight closure of the dura and/or scalp. Progressive neurophysiological loss has, in these instances at least, been stopped. Obviously this manoeuvre does increase temporarily the intracranial tension. This disadvantage was controlled by the methods described.

CONCLUSIONS

No positive conclusions are drawn from the small series of cases presented. Obviously the data are incomplete, particularly those of the laboratory, as is inevitable under the circumstances. However, it would seem from the results obtained that this method of control of hernia cerebri is deserving of further trial.

SUMMARY

Six cases are presented, one of brain abscess and five of hernia cerebri, in which the hernia was successfully retained and subsequently reduced by tantalum cranioplasty. In three of these instances previous conservative treatment had failed in this attainment.

TIGHT DURAL CLOSURE WITH PEDICLED GRAFT IN WOUNDS OF THE BRAIN

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ALTHOUGH the importance of not opening the dura unnecessarily has been fully recognized both in regard to cerebral dura[2,10] and spinal dura for some time, inadequate attention has been devoted to its repair in cases of penetrating wounds of the brain. The necessity for careful repair of the laceration of the dura in the region of the cribriform plate or one of the paranasal sinuses has long been known by neurologic surgeons.[6] On the other hand, deliberate meticulous repair of a laceration of the dura under the vault of the skull has not generally been recognized in the literature,[1,2,3,5,9] although Spurling, Senior Consultant in Neurosurgery in the European Theater of Operations,[8] has recommended the use of grafts whenever it is impossible to close the dura with interrupted sutures. Usually dural patches have been free grafts of fascia lata, pericranium or temporal fascia. Pedicled grafts, having their own blood supply, would appear more likely to take, especially in the presence of bacteria. Insofar as the author is aware, the use of pedicled grafts for this purpose has not been previously reported.

THE NEED FOR WATERTIGHT CLOSURE OF THE DURA

Watertight closure of the dura is a barrier in two senses: it excludes blood and bacteria from the central nervous system, and it restrains cerebrospinal fluid and brain within their normal confines. In the past, closure of the galea aponeurotica has been emphasized to the neglect of the dura mater. From the surgical point of view, the dura is analogous to the serous membranes in other parts of the body. Naturally, closure of the scalp is important, but when the dura is properly closed, scalp closure regains its proper position of secondary importance. Careful restitution of the dura provides an effective barrier between the central nervous system and the somatic tissues. In the absence of a portion of the skull and scalp, as happens all too frequently in war wounds, the repaired dura alone may be the only effective barrier that excludes from the central nervous system both bacteria and blood. The former are the obvious source of intracranial infection: meningitis, brain abscess and encephalitis. The latter acts as nourishment for any organisms that may be present, and itself is organized into meningocerebral adhesions.

In the absence of scalp due to direct trauma, infection, or ischemic necrosis, the well-repaired dura provides a base for granulation tissue in the case of a small scalp defect, or a substratum for grafting of skin in the case of larger scalp defects. In the event that the brain has been inadequately

debrided at the time of the primary operation, it allows the infection to become localized as an abscess, which can be dealt with by block excision after the scalp has healed.

A properly closed dura contains the cerebrospinal fluid. The outpouring of this fluid tends to impair the healing of the scalp and keeps open the direct route to intracranial sepsis. The well-closed dura also prevents herniation of the brain, which is recognized[7] to be due primarily to dural defect, and its more serious sequel, cerebral fungus. Naturally, a good scalp repair is an excellent support for dural closure.

MATERIALS

Inasmuch as the calvarium is almost a hemisphere, its coverings are ideally disposed for the rotation of pedicled grafts. Within each lateral semicircular aspect of the vault of the skull there is the smaller semicircle of the temporal fossa with its contained temporal muscle, and the latter's sheath, the temporal fascia. From the center of each of these semicircles, there radiate the temporal arteries. These well-known facts, utilized daily in making horse-shoe flaps of scalp or bone, are equally useful in the planning of pedicled dural grafts.

In cases of wounding of the brain, there will be an occasional linear laceration of the dura that can be tightly closed by simple suture. But in any appreciable defect of the dura, some strong fibrous layer is required to form a patch or graft. Excessive tension of the dura may give rise to epidural bleeding, especially when the fracture line extends from the bony defect across one of the larger dural sinuses. It is probably unwise to use the galea to repair the dura, because of its special relationship to both the mobility and the blood supply of the scalp.

The author has used the following tissues:

1. The loose connective tissue between the galea and the periosteum.
2. Pericranium, or periosteum of the skull.
3. Temporal fascia.
4. Falx.
5. Most commonly, combinations of the first three.

METHODS

1. *Planning.* Before the cranial operation is commenced, one plans not only the exposure and debridement of the brain and closure of scalp and skull, but also the dural repair. Frequently, it is best to hinge the galea and skin of the scalp in one direction and the subgaleal loose connective tissue with underlying periosteum and temporal fascia in another. A bone flap may be hinged in a third direction.

2. *Infiltration of fluid under the galea.* A considerable amount of saline solution or local anesthetic is injected under the galea in order to give thickness to the layer of underlying loose connective tissue. When the tip of the needle is below the galea, it takes relatively little pressure to inject the fluid, a large amount of which, often 50 cc., can be infiltrated without moving the needle. The fewer the insertions of the needle, the less likely is a tear in the periosteum to be used as a flap.

3. *The scalp incision* is made through the galea, but not through the underlying periosteum or temporal fascia.

4. *Cutting against the galea.* As the edge of the scalp is reflected, the knife blade cuts against the galea, thus leaving the underlying loose connective tissue fixed to the pericranium and the temporal fascia.

5. *Delimitation of the edge of the dural defect.* After the defect in the skull is exposed, the edge of the dural defect is found. It may be necessary to rongeur bone peripherally so that a few millimeters of dura are exposed all the way around. It is usually advisable to separate the cerebral cortex where it is adherent. The dural edge is trimmed of frayed tags, and a sharp, clean-cut edge is thus available for repair. A series of fine sutures is placed near the edge. Both ends of each loop of thread are caught in a small hemostat as they radiate from the center of the defect.

6. *Outlining the pattern of the graft.* The graft is now planned so that some combination of subgaleal loose connective tissue, pericranium and temporal fascia can be utilized by rotation or advancement to provide a pedicled dural patch. It may be necessary to undermine the edge of the scalp flap to obtain enough tissue. The base of the graft should be wide enough for adequate blood supply.

7. *The debridement of the brain* is carried out.

8. *The edge of the bone defect is bevelled all around*, or else a ledge is prepared for immediate insertion of a cranioplastic structure. An especially gradual slope is placed on the bony edge over which the graft declines to the dura.

9. *Fixation of the base of the graft.* The pedicled graft is rotated or advanced into place. Its free edge is folded back and its base is sutured with fine silk or nylon to the dural edge. These sutures, which are placed at about 6-millimeter intervals, do not usually go through the whole thickness of the graft.

10. *The rest of the graft is sutured* similarly to the remaining free edge of the dura. When this is completed, one sees the normal pulsations of the brain and there is no leak of cerebrospinal fluid.

11. *Avoidance of pinching the base of the graft.* If there is a bone flap to be replaced or a tantalum plate to be inserted, it is fixed in such a way that it does not pinch the base of the graft and impair its blood supply.

12. *Scalp closure.* In the presence of possible infection, it has been our practice to avoid buried sutures in the scalp. The author has used black silk with a simple through-and-through suture alternating with an end-on mattress suture. Naturally, all threads are at right angles to the wound edges.

ILLUSTRATIVE CASE

The patient was a soldier in his twenties who was wounded in Normandy on June 9, 1944. A shell fragment penetrated the scalp, skull and brain in the left temporoparietal region. Several small metallic fragments remained in the scalp. The patient suffered motor aphasia and right hemiplegia, but was conscious and oriented. The scalp wound was 2 cm. in diameter and there was extensive damage to the galea and the temporal muscle. Smears of the wound showed no organisms. On June 11, 1944, the patient underwent debridement of the skull, scalp and brain, with removal of all depressed bone fragments. The brain was cleansed for a depth of 7 cm. and there was a dural defect almost 7 cm. in diameter. No attempt was made to close the dura. The scalp was closed under considerable tension with heavy silk sutures.

The patient was placed under the author's care in a fixed hospital on June 15, 1944. X-ray films revealed no retained bone fragments in the brain and it seemed as if the scalp wound would heal by primary intention.

However, on June 23, 1944, a cerebral fungus, 2.5 cm. in diameter, appeared between the edges of the scalp wound which had separated (Fig. 1). Smears of the protruded portion of brain revealed only a few diphtheroid organisms and an immediate dural repair was carried out under intravenous anesthesia. The straight vertical temporal incision was re-opened and was continued into the usual temporoparietal horse-shoe incision. The skin and galea were reflected off the underlying connective tissue and periosteum, a pedicled graft of which was

prepared (Fig. 2). The graft was rotated forward and its pedicle sutured with interrupted nylon thread to the edge of the dural defect (Fig. 3). Then the graft was unfolded into place and similarly sutured to the rest of the edge of the dural defect, which measured 5×7 cm. (Fig. 4). The scalp was closed with interrupted silk sutures and without drainage.

On June 24, lumbar puncture revealed slightly yellow spinal fluid under pressure of 300 mm. of water. This fluid contained 108 mgm. of total protein per 100 cc. On June 26, there

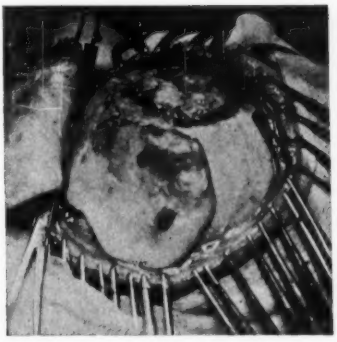

FIG. 1 (*left*). Cerebral fungus immediately after its appearance.

FIG. 2. (*right*). Preparation of pedicled periosteal graft. The galea and skin have been reflected off the periosteum.

FIG. 3 (*left*). The suturing of the base of the pedicled graft to the proximal edge of the dural defect.

FIG. 4 (*right*). Completion of repair of the dural defect with pedicled graft of periosteum.

were 63 mgm. of total protein per 100 cc. and 360 leukocytes per c. mm. On this date, the bacterial cultures of the swabs of the brain made before and at operation revealed no growth.

The convalescence was uneventful except that a portion of the scalp edge, 2 cm. in diameter again became necrotic. However, under moist saline dressings, the defect of the scalp was quickly filled with granulation tissue. The wound was completely healed by the middle of July, at which time the patient was walking about by himself. On July 25, an encephalogram revealed essentially normal ventricles and some air directly under the dural graft. The total protein content of the spinal fluid was 32 mgm. per cent and there were 17 leukocytes per c. mm.

The patient left the author's care on July 28, 1944, at which time he was bright and alert. He understood speech perfectly and was starting to use his right upper limb. He was able to walk well, although with circumduction of the right lower limb. Visual acuity and visual fields were normal.

RESULTS

Pedicled grafts to the dura have been used in the author's complete series of 45 successive battle casualties with loss of dural substance in the summer of 1944. All wounds were caused by shell fragments except two due to explosions and two due to blunt injuries of the skull in the frontal region. There were 18 primary operations and 27 secondary operations. At the same time, there were three additional battle casualties with dural penetration that underwent surgery. Two of these patients had linear tears of the dura which could be sutured without a graft, and one had a very extensive defect with clostridial contamination in which the dura was not repaired. Adequate x-ray and surgical facilities, blood transfusions, sulphadiazine and penicillin were available.

The 18 primary operations were carried out from one day to 32 days, with an average of ten days, after wounding. The surgical procedure usually consisted of debridement of scalp, skull and brain with dural repair. There were retained bone fragments in the brain in every case, and all bone fragments were removed at operation. Organisms were found in the brain itself in ten of these cases, and bacteria were cultured from scalp and skull in eleven. The patients left the author's care from 13 to 58 days after operation with an average postoperative stay of 30 days. There were no cases of encephalitis, brain abscess or meningitis, and in no instance did the dural repair break down. The wounds healed by primary intention in all cases except three in which there was a superficial scalp infection, each of which healed promptly. There were no deaths in this series.

There were 27 secondary operations which were carried out from three to 57 days, with an average of 17 days, after the wounding. Bone fragments were present in the brain in 23 of the 27 cases before operation by the author. All these bone fragments were removed, as far as could be determined both by palpation and postoperative x-ray films. Organisms were found in the brain itself in 17 and in the scalp or skull in 16 of these cases. There were a few cases in which bacterial cultures were not made. The patients left the author's care from 16 to 78 days after operation, with a postoperative stay averaging 34 days. There were four deaths in this series, two of which were from encephalomeningitis due to Gram-negative bacilli before the author began to use urea[4] as an adjunct to sulphonamide therapy of such infections. The third case was that of a man who had an extensive trauma to the basal ganglia on both sides and who had been critically ill ever since his wounding. The fourth was that of an extensive slow hemorrhage in the region of the basal ganglia. There were two other cases of postoperative encephalomeningitis with recovery, and seven cases of superficial scalp infections in all of which the wound proceeded to heal well by granulation.

Failure of Pedicled Graft to be Watertight. There was one case of gross failure of the graft to hold. In an advanced hospital, a transverse incision had been made low in the anterior temporal region. The scalp gaped 5 cm. and cerebrospinal fluid poured forth in large amounts. The dural defect was 8 cm. anteroposteriorly by 12 cm. vertically. There was a defect of 1 cm. in the inferior horn of the lateral ventricle. Because of the original horizontal incision, it was impossible to hinge the periosteal graft inferiorly on the zygoma, which is the most desirable method when repairing defects in this region. The scalp was closed tight under moderate tension. Probably a large pedicled scalp flap should have been depressed into the middle fossa over the dural repair.

There were three other cases out of the 45 where the graft became necrotic due to infection. In three of the four cases, the patient placed his fingers in the wound and there was contamination with Gram-negative organisms.

POSSIBLE COMPLICATIONS

Osteomyelitis. It may be argued that osteomyelitis is more likely to set in if the bone is denuded of pericranium. As a matter of fact, no instance of osteomyelitis was encountered in this series. Furthermore, after a fair experience with this method, it was usually possible to leave 2 or 3 cm. of periosteum at the edge of the bone defect and to swing the graft from tissues from a distance. Finally, even if osteomyelitis should take place, the pus would be sealed from the intradural structures by the graft.

Epilepsy. It is conceivable that suturing mesodermal tissues into the dura would result in meningocerebral scarring, which might give rise to convulsions. On the other hand, it is probable that as soon as the graft is in place, arachnoidal cells grow under the graft and seal its edge. Then, cerebrospinal fluid circulates around the damaged brain and washes away the blood which may be present from capillary ooze after the operation is completed. In fact, there were only two cases of temporary postoperative convulsions in the present series of 48 cases of dural penetration. In one of these, there was bleeding from the superior sagittal sinus. Hence, the element of venous congestion probably entered into the production of the epilepsy. The author believes that the low incidence of epilepsy in this series was due to the deliberate excision of obviously necrotic cortex.

Bone Growth. When periosteum is used for the graft, it is possible that it will produce bone. This would be a desirable result because the dural defect is invariably under an osseous defect. In two cases, a tantalum plate was inserted after the pedicled graft to the dura had been completed. In these cases, the plate bridged the base of the flap and was adequately supported by the edge of the bone around the rest of the defect. Such plates will probably be inserted at the time of brain debridement more frequently in the future.

SUMMARY

The importance of precise closure of the dura mater over either vault or base of the skull is emphasized. A procedure for repair of the dura with pedicled grafts of the subgaleal loose connective tissue, pericranium and temporal fascia is described and illustrated. The results of dealing with a consecutive series of battle casualties in which such dural repair was done are recorded.

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OBSERVATIONS ON INFECTION IN PENETRATING WOUNDS OF THE HEAD

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THE PREVENTION and control of infection in penetrating head wounds forms the basis of much of the treatment from the time of injury until healing occurs and is one of the major responsibilities of the Army neurosurgeon. The almost universal employment of sulfonamides and penicillin has resulted in material changes in the frequency, the symptomatology, the course, and the outcome of wound infections. These changes in turn have modified the surgical treatment of cranio-cerebral injuries and their sequelae. The following observations relative to these modifications are based upon clinical experiences in a fairly large series of battle casualties seen in a neurosurgical center in the first five months following the landings in Normandy. At the present time a statistical analysis of these cases is not possible. It is convenient to consider separately wound infection, meningitis, and brain abscess.

WOUND INFECTION

Approximately 15 per cent of the head wounds showed some degree of infection. Gross involvement of the brain with the formation of cerebral fungus has been infrequent, particularly since the first month. With very few exceptions the wound infections appear to be due either to incomplete debridement of the missile tract, particularly failure to remove all indriven bone fragments, or to closure of the scalp under excessive tension. In a few instances the wound breaks down from no apparent cause other than excessive contamination.

It is frequently difficult to tell whether a wound is healing properly since under the influence of chemotherapy the characteristic signs of infection may be absent. Local swelling may be the result of cerebral herniation through a dural defect, subgaleal cerebrospinal fluid collection, hematoma, edema of the scalp, or pus. Redness of the scalp rarely occurs and tenderness is so deceptive as to be of little diagnostic value. Thinning and darkening of an apparently healed scalp incision has frequently been the only evidence of an underlying collection of pus. Furthermore, the usual signs of systemic reaction to infection, such as fever and leukocytosis, are rarely present until the process is well advanced. Not infrequently judicious exploration of the wound with a small instrument may be the only method of establishing the diagnosis. If the wound is clean this does not seriously delay healing.

The treatment of these infections consists essentially in the establishment of adequate drainage, and the intensive local and systemic use of

chemotherapy. In most instances the wound must be widely reopened to prevent the development of pockets of pus and extension of the infectious process to the deeper structures. Penicillin has been effectively employed locally in solution (10,000 units per cc. of saline) through a Dakin tube laid in the wound and carried out through the dressing. This method permits the frequent instillation of the drug (usually 10,000 units every three hours) and can be carried out satisfactorily by the nursing staff. It has the further advantages of permitting aspiration of pus from the wound before each instillation, and of securing adequate distribution of the drug throughout even a deep wound. Inasmuch as the tube represents foreign material in the wound and a possible avenue for secondary infection, it seems preferable not to allow it to remain in place for more than one week. In the presence of a cerebrospinal fluid leak the tube should not be placed in the depths of the wound since a fistulous tract may form about it. Dry penicillin mixed with sulfanilamide crystals (5 to 10,000 units of penicillin to each gram of sulfanilamide) has been dusted into the wound as an alternative method of local application. This method permits greater concentration of the drug within the wound with less loss through the dressing. However, it has the disadvantage of requiring frequent dressings. In our experience daily replenishing of the drugs has proven adequate for most wounds.

In all cases both penicillin and sulfadiazine have been employed systemically. Penicillin has been given intramuscularly in doses of 10,000 units every three hours in the average case. In critical cases both the dosage and the frequency of administration have been increased. Sulfadiazine has been employed in the usual doses and followed by blood level determinations.

MENINGITIS

Meningitis is one of the most serious complications of penetrating wounds of the head and in our series has occurred in approximately 4.5 per cent of the cases. The likelihood of its occurrence is dependent to a large extent upon the course of the missile and it is convenient to consider separately those cases in which the wound involved the vault of the skull alone and those in which there was associated perforation of the orbit or the paranasal sinuses.

An infected wound may serve as the source of meningitis in the presence of an open dura mater, particularly when there is direct communication with the subarachnoid space or ventricular system (Case 1). Infection in the wound even with exposed cortex is rarely followed by meningitis or extensive cerebritis unless there is a discharge of cerebrospinal fluid. Under these circumstances revision of the wound, including repair of the dural defect, should be carried out without delay. We have come to believe that even in the presence of an already established meningitis constant re-infection can be avoided only by prompt closure of the cerebrospinal fluid fistula even if a fascial graft is necessary. In this type of case the intraventricular administration of penicillin may be of great value.

Missiles entering the skull after passing through the orbit or paranasal sinuses must always be regarded as a greater potential source of infection than those entering the vault directly. In these cases meningitis may occur in the absence of an obvious cerebrospinal fluid leak. While it is not advisable to attempt the removal of all such missiles, these patients warrant prolonged and careful observation even when they appear to be symptom-free (Case 2). When rhinorrhea or otorrhea is associated with this type of wound the pathway for infection is enlarged. However, if adequate chemotherapy is maintained surgery may be delayed for a few days to allow for possible spontaneous closure. Unfortunately the wounds that cause rhinorrhea almost invariably include large defects of the paranasal sinuses, the floor of the skull, and the overlying dura mater, and consequently rarely close spontaneously. Frequently the intracranial damage disclosed at operation is much more extensive than one would be led to suspect by the x-rays or the external wound, and repair is a formidable procedure which may not always be successful at the first attempt.

The clinical picture produced by early meningitis following a penetrating wound of the head is not always clear-cut. Sometimes relatively little febrile reaction is shown and the patient may not appear acutely ill. Diagnostic nuchal rigidity is difficult to distinguish from the meningismus that is so frequently present following this type of head injury. Not infrequently a chill or convulsion is the initial symptom. Whether the presence of meningitis is merely suspected or is more clearly indicated by a fulminating onset, spinal puncture should be done without delay. If the fluid is cloudy it has been our practice to institute all types of treatment at once including instillation of penicillin at the time of the initial puncture. Despite the marked pleocytosis which is usually present, culture of the fluid frequently shows no growth. However, this is not regarded as an indication for altering the treatment.

The plan of therapy to be followed in cases of meningitis associated with head wounds will obviously vary somewhat from patient to patient, but certain general lines of attack are common to all. In our opinion it is of primary importance to eliminate the source of the infection unless this involves a very extensive operative procedure. Frequently less formidable procedures are not only well tolerated but make the difference between success and failure of the treatment by the prevention of re-infection. Wide opening of an infected wound, removal of a necrotic cerebral fungus, repair of a cerebrospinal fluid leak, are all examples of active therapy directed at the seat of the infection. Second in importance is the maintenance of adequate chemotherapy. Sulfadiazine in doses of 1.0 to 1.5 gm. every six hours will usually maintain an adequate blood concentration but in the presence of well established infection this must be increased. The six-hour interval has been adopted to synchronize the administration with intramuscular injections of penicillin (usually in doses of 10,000 units) every three hours. Because of the rapid elimination of the latter drug patients in critical condition

have been given 20,000 units every two hours. In connection with this systemic therapy it may be necessary to administer a soluble preparation of sulfadiazine intravenously when the patient is stuporous or uncooperative and if this is done the penicillin can be introduced by the same route.

Penicillin when introduced directly into the cerebrospinal fluid is an extremely valuable addition to the armamentarium against meningitis. We have used it in doses up to 50,000 units every twelve hours in the more serious cases. Certain preparations appear to be moderately irritating to the spinal roots for a few moments after the injection, but no ill effects have been observed and this reaction has been lessened by the use of saline solution as a solvent rather than distilled water. The possible failure of the drug to reach all parts of the cerebrospinal fluid pathways in effective concentration must be borne in mind, and if the patient fails to show a satisfactory response within 48 hours, intraventricular administration should be begun promptly. In most instances this is not difficult and can be done at twelve-hour intervals through posterior parietal or frontal burr holes. The latter location has some advantages in that the taps are more easily performed and there is at least theoretical ground for believing that the preparation would be less apt to drain out along the tract of the ventricular cannula.

Obviously the effectiveness of the treatment of meningitis hinges to a great extent upon the causative organism. If it is penicillin-resistant the prognosis becomes much worse. In our cases mixed infections that included organisms of the colon group produced the most dangerous meningeal infections.

Case 1. *Penetrating wound of left parieto-occipital region from shell fragment with indriven bone fragments. Nine days after injury sudden onset of meningitis due to penicillin-resistant organisms, with death in three days.*

This infantryman was wounded in the left parieto-occipital region by a shell fragment on 29 August 1944 in France. Partial debridement of the wound was carried out on 30 August 1944 at an Evacuation Hospital, at which time the foreign body and a few of the indriven fragments were removed. The dura was left open. On admission to the 160th General Hospital on 4 September 1944 examination disclosed a right homonymous hemianopsia, mild mixed aphasia and mental confusion. There was a wound in the left occipito-parietal region which was healed except for its lower angle, from which a few drops of purulent material could be expressed.

X-ray examination revealed a 5-cm. defect in the left parieto-occipital region with many small bone fragments situated about 6 cm. beneath the opening (Fig. 1).

In spite of the superficial infection in the wound and the occasional drainage of a few drops of clear fluid the soldier was afebrile. Although he was placed on a regime of sulfadiazine and penicillin on the third hospital day he developed a severe headache and rise in temperature. Lumbar puncture at this time showed cloudy fluid, and 30,000 units of penicillin were injected intrathecally. Because his condition did not improve after 24 hours of intensive chemotherapy, intraventricular administration of penicillin was begun. Despite these measures the patient's condition became steadily worse, he became comatose, and died three days after the onset of the meningeal infection. Culture of the spinal fluid showed a mixed infection with predominance of B. coli.

Comment. In this case the presence of an unrepaired dural defect permitted intracranial extension of a superficial wound infection. Unfortunately

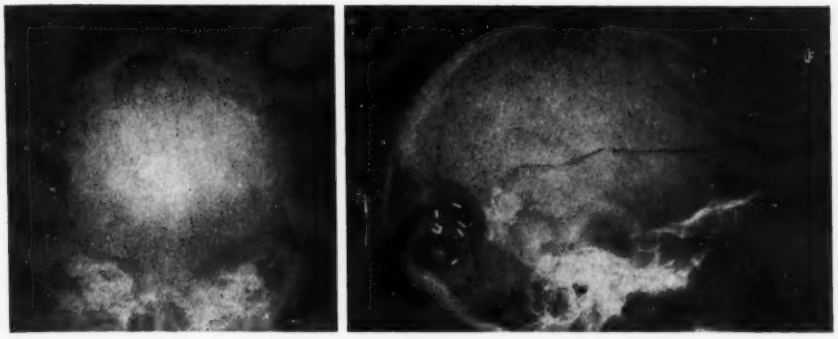

FIG. 1. Case 1. Films following original debridement, showing residual skull defect and intracerebral bone fragments.

the predominating organism was resistant to chemotherapy. It is noteworthy that the spinal fluid leak was both intermittent and inconspicuous and the wound infection mild.

Case 2. *Penetrating wound of left temporal region due to large shell fragment which lodged in region of sphenoid sinus. Sudden onset of meningitis two and one-half weeks following injury. Removal of foreign body through nasal approach followed by transient rhinorrhea. Recovery from meningitis under intensive chemotherapy.*

This 19-year-old infantryman was wounded by a shell fragment in France on 28 August 1944. The fragment entered the left temporal region just posterior to the outer canthus of the left eye. It penetrated medially, passing through the lateral aspect of the orbit and anterior portion of the middle cranial fossa to lodge in the region of the posterior ethmoid and sphenoid sinuses. Debridement and closure of the local wound was done on 28 August 1944 in an Evacuation Hospital and subsequently the left eye was enucleated. The soldier was admitted to the 160th General Hospital on 7 September 1944 with a healed wound overlying a 4-cm. bone defect in the left temporal region. Neurological examination disclosed only deafness in the left ear. The patient's left nostril was obstructed and there was no evidence of rhinorrhea

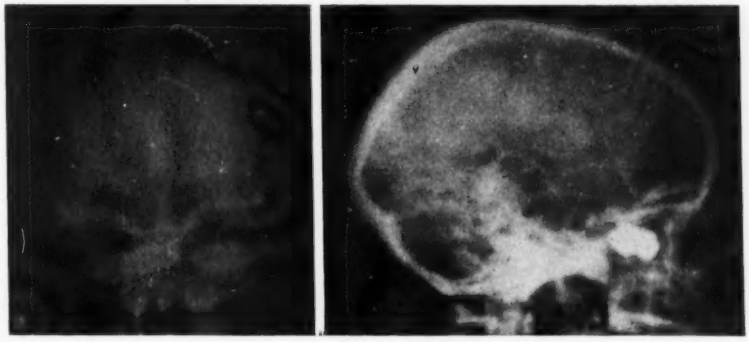

FIG. 2. Case 2. Films showing large shell fragment in region of sphenoid and ethmoid sinuses.

even when his head was hung low over the edge of the bed. Temperature, pulse and respirations were normal.

X-ray examination disclosed fractures involving the lateral wall and roof of the left orbit and the left zygoma. A metallic foreign body about $1\frac{1}{2} \times 3 \times 3$ cm. was seen in the region of the sphenoid sinus and left posterior ethmoid cells (Fig. 2).

Examination of the x-ray films made it evident that the foreign body could be removed more expediently through an intranasal approach than through a craniotomy opening. This was concurred in by an otolaryngological consultant (Major Frank D. Lathrop) who planned to operate 14 September 1944. On the morning of the operation the soldier developed a severe chill and elevation of temperature, indicating the likelihood of meningitis, but nevertheless it was felt advisable to remove the foreign body. Submucous resection, removal of the rostrum of the sphenoid sinus and a portion of the left ethmoid sinus gave access to the shell fragment. During operation there was no evidence of cerebrospinal fluid leak.

TABLE 1

Case 2.—Spinal fluid examinations during therapy

Date	Time	Cell Count	Polys	Lymphs	Smear	Culture	Blood Sulfa Level
14 Sept.	A.M.	42,650	95%	5%	Neg.	Gram-positive, chain-forming cocci	—
14 Sept.	P.M.	18,600	95%	5%	Neg.	Gram-positive chain-forming cocci 24 hours	—
15 Sept.	A.M.	—	—	—	Neg.	Neg.	11.2 mgm.
16 Sept.	A.M.	14,850	86%	14%	Neg.	Neg.	—
16 Sept.	P.M.	10,000	95%	—	Neg.	Neg.	—
17 Sept.	—	6,976	28%	72%	—	No growth in 7 days	—
18 Sept.	A.M.	3,450	—	—	Neg.	No growth in 6 days	—
19 Sept.	P.M.	2,250	70%	30%		Neg.	4.8 mgm.
21 Sept.	P.M.	3,450	—	—	—	—	—
22 Sept.	—	71	67%	33%	Neg.	Neg.	—
28 Sept.	—	—	—	—	—	—	6.2 mgm.%

Immediately following operation lumbar puncture disclosed a spinal fluid pressure of 300 mm. of water and purulent fluid containing approximately 43,000 cells per c. mm. There were mild nuchal rigidity, extreme restlessness, marked confusion and disorientation, and elevation of temperature. Smear of the spinal fluid disclosed no organisms but culture grew out gram-positive, chain-forming cocci which could not be sub-cultured.

The soldier was placed upon a regime of intensive chemotherapy. Because of the mental state, oral medication was not possible, and sodium sulfadiazine was given intravenously. Penicillin was administered intramuscularly in doses of 10,000 units every three hours and intrathecally in doses of 40,000 units every twelve hours. The intrathecal administration of penicillin was begun at the time of diagnostic puncture, and spinal fluid taken 24 hours later showed no growth on culture. Although the spinal fluid cleared rapidly (Table 1), the soldier's mental state became normal only after about two weeks.

At the present time there is no evidence of rhinorrhea and the soldier is up and about with no apparent serious sequelae.

Comment. This case demonstrates that meningitis may develop long after injury and in the absence of rhinorrhea or other obvious avenues of infection. Although the meningitis was recognized at an early stage, operation was not deferred in view of the importance of removing the principal source of infection.

BRAIN ABSCESS

Brain abscess presents a more serious problem than does meningitis, not only because of its higher mortality, but also because of the greater incidence of serious sequelae following successful treatment. The problems associated with prevention are no less difficult than those related to diagnosis and treatment. Adequate debridement of the wound at the time of primary operation is the greatest factor in the prevention of brain abscess. For obvious reasons, this is not always possible, and occasional patients are seen with well-healed wounds but with retained intracerebral bone fragments. It is generally agreed that local abscess formation is much more likely to occur about bone fragments than about metallic foreign bodies. In our experience, approximately 25 per cent of the patients with retained bone fragments developed brain abscesses within six weeks (Case 3). It has been our custom to remove all retained bone, except in those instances in which a single small fragment is deeply situated in an otherwise well-debrided wound. In the latter instance, the trauma incident to the operation would seem out of proportion to the likelihood of the development of an abscess. This policy has been based upon the feeling that abscess formation is not due entirely to the retained bone *per se*, but that the presence of a large number of fragments is a general index of a poorly debrided wound, often containing considerable devitalized brain, blood clot and other foreign material.

In the development of brain abscess following a head wound the well-known clinical picture may be seen, but more frequently both the early stages and the course of the disease are atypical and insidious. Progressive neurological signs rarely develop because the lesion occurs in cerebral tissue already traumatized. Hence more reliance must be placed upon less definite symptomatology, such as irritability, mental sluggishness, increasing severity of headache, or sudden rise in temperature. The appearance of any of these or other vague signs in a patient who has been previously convalescing satisfactorily must be regarded as suspicious, particularly when x-ray shows any type of retained foreign body. Increased intracranial pressure, when present, may be manifested by bulging of the wound, increased spinal fluid pressure, or mild papilloedema. A large proportion of the patients, however, show no evidence of intracranial hypertension even in the presence of a relatively large abscess, a clinical anomaly which is probably due to the increased room for expansion provided by the destruction of tissue incident to the wound. In other instances the lack of pressure symptoms or signs is due to the small size of the lesion, which may consist of a small purulent collection discovered only at operation for secondary debridement. In general the paucity of clinical changes in these cases and the silent nature of the lesion must be borne in mind constantly. In two of our cases the initial symptom was a convulsion incident to the rupture of the abscess into the ventricular system (Case 4).

Increase in the spinal fluid cell count, while suggestive of an abscess, is of less diagnostic significance in battle casualties because of the frequency of pleocytosis secondary to the wound itself.

Although the diagnosis of brain abscess in war wounds presents different problems from those seen in civilian practice, the fundamental principles of treatment remain essentially the same. It has been our practice to establish drainage at the earliest opportunity and it has not been necessary to delay operation to allow for firm encapsulation or sealing off of the overlying subarachnoid space. Adequate exposure of the abscess cavity with minimal exposure of the surrounding cortex is of extreme importance. It is of great value to examine the interior of the lesion by direct vision, not only to insure the removal of all foreign bodies but also to recognize and drain any loculations or secondary abscesses. In addition the identification of small spicules of bone may be aided by digital exploration.

Following the complete evacuation of the abscess and the removal of all foreign bodies we have usually established drainage by the use of a Penrose sheath, or rubber tissue drain, or occasionally by a soft rubber tube. In addition, a Dakin tube with pointed end and supplementary enlarged openings in its walls is introduced into the depths of the cavity. At this time a mixture of dry penicillin and sulfanilamide is placed in the cavity. In contra-distinction to the ordinary practice of leaving the wound entirely unsutured it has been found feasible, with the aid of chemotherapy, to carry out a nearly complete closure in many cases. This has included the repair of the dural defect with a fascial graft which is left unsutured at one point for the drain and Dakin tube. If possible the original scalp wound is sutured and drainage effected through a stab wound.

The exact technique of drainage must be dependent upon the site, the depth, and the character of the wall of the abscess. In some instances it has been possible to use marsupialization when the wall is well organized and the lesion is near the surface. However, it has been noted that in general the capsule is thin and poorly organized. Presumably this is the result of a combination of factors including previous chemotherapy, decreased reactivity in the area of traumatized brain, and the relatively early stage in which some of the abscesses are seen.

Postoperatively these patients merit careful observation and attention, particularly in respect to the maintenance of adequate chemotherapy, the early detection of complications, and the inspection of the wound to insure that drainage is not obstructed. Sulfadiazine by mouth to maintain an effective blood level is essential. Penicillin is routinely used intramuscularly and locally through the Dakin tube, and if any evidence of meningitis appears it is injected intrathecally as well. The Dakin tube is led out through the dressing and is either covered with a separate piece of sterile gauze or sealed by inserting the end of a sterile medicine dropper into the opening. The nurse may be instructed to carry out gentle aspiration of the tube before each injection of penicillin. The time of removal of the Penrose sheath or rubber tissue drain depends upon the amount of drainage and the clinical course. In the average case there is surprisingly little drainage postoperatively and it has been our practice to remove the drain after about four days. The Dakin

tube is usually left for an additional one or two days and is then withdrawn until it lies beneath the scalp, where it is allowed to remain for another twenty-four hours, thus insuring the direct treatment of any subgaleal infection. In a few cases there has been a delay in healing of the scalp wound requiring local penicillin treatment for a longer period.

Case 3. *Penetrating right parietal wound from mortar shell fragment. Debridement of wound followed by prompt healing in spite of retained intracerebral bone fragments. Increased headaches and slight exaggeration of left hemiparesis about three weeks after injury. Removal of bone fragments and drainage of abscess followed by satisfactory recovery.*

This soldier sustained a penetrating wound of the right parietal region from a mortar shell fragment on 27 July 1944 in France. Debridement and closure of the wound was done on the day following injury at an Evacuation Hospital. Some penetration of the right parietal lobe

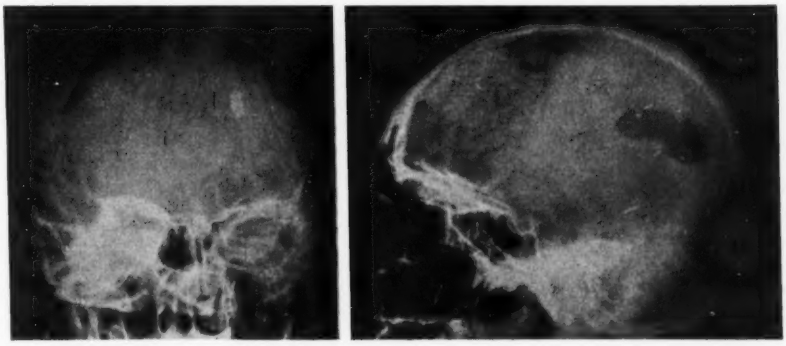

FIG. 3. Case 3. Films following original debridement, showing residual skull defect and intracerebral bone fragments.

was found and damaged brain, metallic fragments and bone fragments were removed. The dural defect was not repaired.

On admission to the 160th General Hospital five days after injury the soldier showed a clean wound and an incomplete flaccid, left hemiplegia, which was slowly improving.

X-ray examination revealed a bone defect in the right posterior parietal region measuring 5×2 cm. About 4 cm. deep to the opening several small bone fragments were visualized (Fig. 3).

The soldier improved sufficiently to walk about the ward, but about three weeks after injury he began to complain of headaches and slight increase in the weakness of his leg. Secondary debridement of the wound was carried out on 28 August 1944 at which time a well-encapsulated abscess was found containing the bone fragments. The abscess was evacuated, all fragments were removed, a mixture of dry penicillin and sulfanilamide was instilled in the cavity, and a Dakin tube was carried out from the lesion through a stab wound in the scalp. The dural defect was repaired with a fascia lata graft leaving one margin open for the tube. Liquid penicillin was instilled through the tube and the drug was also given intramuscularly and intrathecally for the first 48 hours. Sulfadiazine was administered in the usual doses. The tube was withdrawn from the abscess cavity to a point beneath the scalp after two days and removed entirely at the end of five days. The wound healed promptly and the soldier's condition remained good throughout. Culture taken at operation showed no growth after six days. Following operation the patient's headaches disappeared and the strength in his left side began to return rapidly. He was transferred to the Zone of Interior on 16 September 1944.

Comment. In this case a dural defect measuring approximately 5×2 cm. was closed with a fascia lata graft despite the finding of an abscess. An adequate avenue for drainage as well as for the instillation of penicillin locally was provided by a single Dakin tube carried out of the cavity through a small opening along the margin of the graft. Healing occurred promptly, uncomplicated by spinal fluid leak.

Case 4. *Shrapnel wound through right orbit into left frontal lobe with retained shrapnel ball. Right eye enucleated. Occasional mild headaches but no other symptoms or signs. Eighteen days after injury sudden onset of convulsions and death. Left frontal abscess with rupture into ventricle disclosed at autopsy.*

On 4 July 1944 this soldier sustained multiple shrapnel wounds including a penetrating wound through the right orbit into the left frontal region. On 9 July 1944 the right eye was enucleated at an advance hospital in France, and on 14 July 1944 he was transferred to the 160th General Hospital.

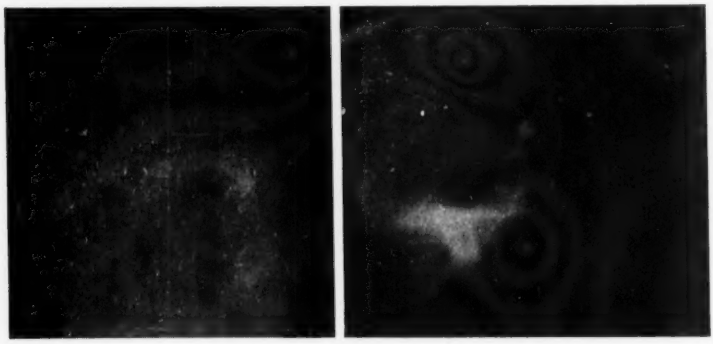

FIG. 4. Case 4. Films showing shrapnel ball in left frontal region.

Temperature, pulse and respirations were normal and neurological examination disclosed no changes. X-rays revealed a shrapnel ball in the left frontal lobe (Fig. 4), but in view of the good condition of the soldier and the absence of any indriven bone fragments its removal was not considered advisable. The soldier was active on the ward, went to mess, and had no complaints other than occasional headache. On 22 July 1944, 18 days after injury, he suddenly developed severe convulsions and died within three hours.

Autopsy revealed a poorly encapsulated left frontal abscess in the medial and inferior portion of the left frontal lobe. Rupture into the frontal horn of the left lateral ventricle had occurred with rapid spread of pus throughout the ventricular system.

Comment. This case emphasizes the silent nature of certain abscesses and the necessity for constant vigilance in their diagnosis. It has been our experience that infection is more prone to occur around the larger metallic foreign bodies and their removal seems advisable in all cases where they are relatively accessible.

SUMMARY

An attempt has been made to present the principal differences we have observed between intracranial infections associated with war wounds and

those previously encountered in civilian practice. The infected wounds have been characterized by only mild local and general reactions, have responded promptly to local and general chemotherapy, and have usually healed rapidly following early secondary closure. It has been apparent that the occurrence of meningeal infection is not only dependent upon the completeness of the primary debridement but also the relation of the missile tract to the paranasal sinuses and orbits. The eradication of all sources of continual reinfection seems to be a prerequisite to the successful therapy of the meningitis. The use of penicillin intrathecally or by the intraventricular route has proven surprisingly effective in a large proportion of the cases. Of the brain abscesses encountered a striking percentage have been clinically silent, many reaching considerable size with little evidence of increased intracranial pressure. Complete evacuation of the abscess in combination with intensive local and systemic chemotherapy has proven effective in most cases.

NEW USES OF TANTALUM IN NERVE SUTURE, CONTROL OF NEUROMA FORMATION, AND PREVENTION OF REGENERATION AFTER THORACIC SYMPATHECTOMY. ILLUSTRATION OF TECHNICAL PROCEDURES*

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TANTALUM is a metal that causes practically no irritation on the part of human tissues.[4,5] It has the added advantages of easy processing into plates, thin sheets, or wire at the factory, and of convenient sterilization, drilling, shaping, or cutting in the operating room. For use in operations on the nerves it is available† in thin sheets (0.001 and 0.002″), in annealed rolls (approximately 0.00075″) of convenient size for wrapping a nerve suture or an area of neurolysis, and in thinner foil (0.00025″). The latter has turned out to be too thin, having such a tendency to crumple and fragment that it has had to be discarded. For the past two years, before they were made available for commercial use, these products were extensively used and tested by the neurosurgical specialists in both the Army and Navy Medical Corps.

This paper presents adaptations of these new tantalum products which have proven to be of value in the operative treatment of severed peripheral nerves, painful neuromas, and in thoracic sympathectomy. These procedures can best be described by a series of simple sketches and reproductions of x-rays, with accompanying brief comments in the text.

NERVE SUTURE

Current statements to the contrary, even the finest silk sets up a definite amount of fibrosis when used as epineurial sutures,[5] and occasionally may produce a severe reaction. Under the most favourable circumstances a thin capsule of connective tissue is clearly visible to the naked eye around each silk knot, and in occasional instances the strands may be pushed apart by a dense mass of fibroblasts, as illustrated in Fig. 1.

Granted that the surgeon has good eyesight, 0.003″ tantalum wire swedged onto fine atraumatic needles is the ideal material for suturing severed nerves. Finer than any other available stitch and also definitely less irritant to tissue,[4,5] it is easy to tie and there is no tendency of the first half

* This article has been released for publication by the Division of Publications of the Bureau of Medicine and Surgery of the United States Navy. The opinions and views set forth are those of the writers, and are not to be construed as reflecting the policies of the Navy Department.

† These products can now be obtained for limited civilian use from the Ethicon Suture Laboratories of Johnson & Johnson at New Brunswick, N. J.

hitch of a square knot to slip. For this reason a slight but perceptible degree of trauma is avoided every time a suture is tied. The fact that this fine wire breaks when put under unnecessary tension is an added safeguard. A further unique advantage is tantalum's relatively high opacity to x-rays, so that each delicate knot remains as a clear marker of the position and state of the line of anastomosis.

Colonel R. Glen Spurling,[9] formerly in charge of neurosurgery at the Walter Reed General Hospital in Washington, and Lt. Colonel Barnes

FIG. 1. Fibrosis in nerve following suture with silk. This photomicrograph enlarged 40× shows a silk knot cut across on the right, and a silk strand in cross section on the left. Note the separation of the individual silk strands by fibrous tissue and the degree of surrounding fibrosis. This section was taken from a fusiform neuroma that developed at the site of suture of an ulnar nerve with laceration of the surrounding tendons at the wrist. There was no history of sepsis to account for this severe fibrosis. (We are indebted to Lt. Comdr. Shields Warren (MC), U.S.N.R., for this photomicrograph.)

Woodhall, his successor, first experimented with covering the line of a nerve suture with tantalum foil 0.00025″ in thickness. It was soon discovered that foil tended to break up because of its extreme thinness and it was therefore discarded, although the early results were promising. Woodhall and other neurosurgical specialists in both the Army and Navy then utilized annealed sleeves of sheet tantalum 0.00075″ in thickness, which were prepared for us by Professor Paul Weiss of the University of Chicago. Still more recently these annealed rolls of sheet tantalum have come into commercial production. Under proper circumstances, this method of protecting the area of nerve

anastomosis appears to be of definite value. This type of suture has now been used in 22 cases at the U. S. Naval Hospital at Chelsea over the past eighteen months, and this experience has led to several minor improvements in technique, which are illustrated in Fig. 2.

In this figure the annealed roll of tantalum (0.00075″ thick) has been slipped over the proximal or distal stump before the nerve is sutured. On completing the suture it is drawn over the area of anastomosis. It can equally

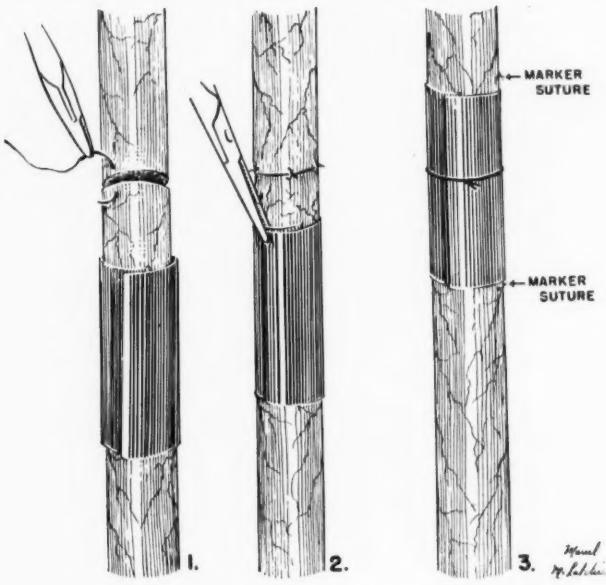

FIG. 2. Application of tantalum sleeves to protect area of nerve suture. (1) and (2) Epineurial sutures of 0.003″ tantalum wire swedged on fine needles are used to approximate the freshened nerve ends. The sleeve of annealed tantalum is placed over one end of the nerve pending the completion of the suture and then drawn over it. The springiness of tantalum rolls annealed in an electric furnace permits the alternative method of their being opened and slipped around the completed suture. (3) After application the tantalum sleeve is loosely snugged to fit the nerve trunk with one or two ties of 00 plain catgut. Additional marker sutures of tantalum are placed at 1 mm. from each end of the sleeve.

well be unrolled and slipped as a sheet beneath the completed line of suture. On release it recoils into its previous cylindrical form and can then be gently snugged up against the nerve trunk by one or more circular ties. These should be of 00 plain catgut and must never be tied tightly. At first silk or tantalum ties were used by a number of surgeons, with resultant impaired rate of regeneration. Re-exploration showed that the central stump of the nerve had swollen slightly and was constricted by the encircling metallic cuff. This has occurred twice in my own experience, but never since fine, rapidly absorbable catgut has been used.

Fig. 2 (1) shows marker sutures of fine tantalum tied in a loose single knot through the epineurium just beyond each end of the tantalum sleeve. With this recent modification an x-ray can always establish the exact position of

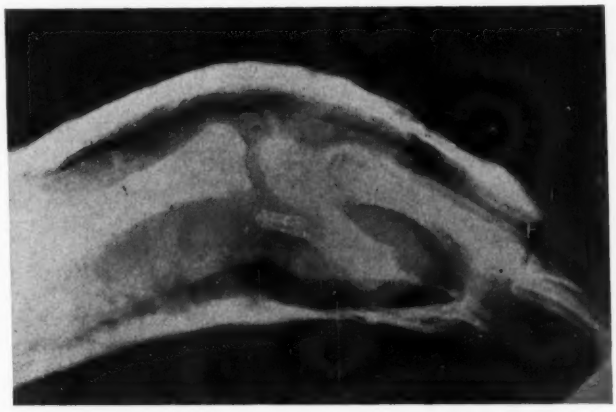

FIG. 3. Position of metallic sutures indicates that nerve ends remain in good approximation. The photograph of this x-ray has been slightly retouched in order to pick out the metallic sutures, as these are too fine to reproduce well.

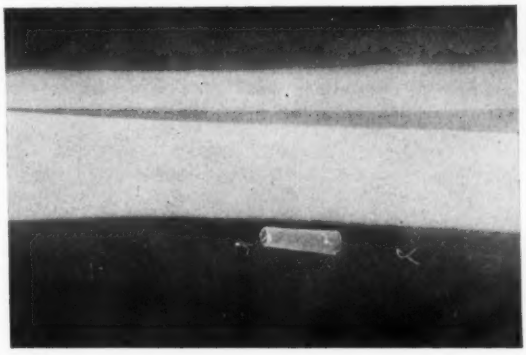

FIG. 4. Evidence of separation of sutured ends of nerve. At operation tantalum sutures were placed similar to those illustrated in Fig. 3. The gap between the nerve ends is shown not only by the shift of the actual epineurial stitches within the sleeve but also by the marker sutures. Note the extensive shift of the marker suture on the right. In spite of the fact that separation of approximately 1 cm. is shown, the nerve ends remained within the sleeve and very satisfactory regeneration has taken place across the gap. The photograph of this x-ray film has been slightly retouched in order to make the fine metallic sutures visible.

the anastomosed nerve ends. At first glance these extra marker sutures may seem unnecessary, because a displacement of the metallic strands at the suture line should show its separation. It is quite possible, however, for all the torn out sutures to remain attached to one end of the nerve and thereby

fail to demonstrate its separation. The roentgenogram reproduced in Fig. 3 was taken immediately after operation to ascertain the condition of a suture in the ulnar nerve. In this instance the ends of the nerve had been sutured with moderate tension under local anaesthesia. As the anaesthesia had worn off prior to closure of the incision, the patient was lightly anaesthetized with sodium pentothal. In the course of the application of a plaster bandage in flexion, the patient forcibly extended his wrist. All fears that the sutured nerve ends could have been pulled apart were dispelled upon viewing the film. In contrast, Fig. 4 shows distinct evidence of separation of a sutured

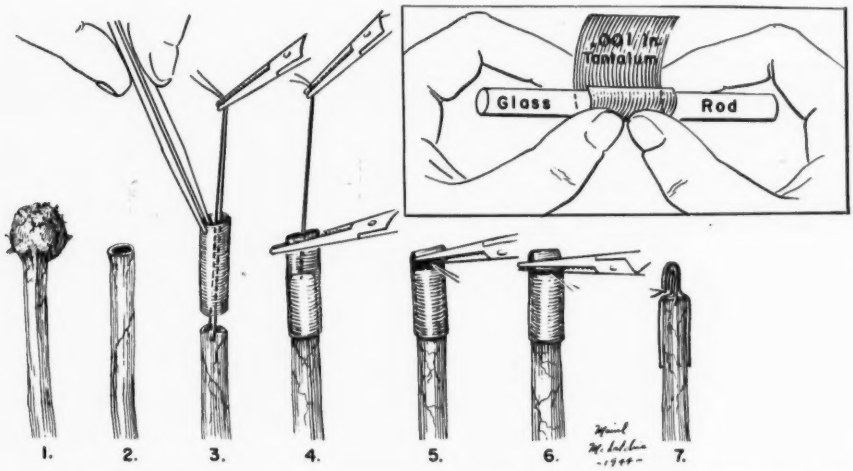

FIG. 5. Application of tantalum cap to stump of nerve for prevention of neuroma formation. (1) and (2) Resection of painful end-bulb neuroma. (3) The amputated end of the nerve is transfixed by a fine silk stitch and covered by a sleeve of tantalum. (4) The open end of the sleeve is crushed in a hemostat. (5) and (6) The flattened end is turned back on itself and crushed again, thereby fixing it firmly to the end of the nerve.

posterior tibial nerve, which followed the development of a large pulsating false aneurysm from an undiscovered laceration in the side of the peroneal artery.

Another helpful use of tantalum in nerve repair is for marker sutures whenever the site of injury may need to be re-explored, as in securing severed nerve ends exposed in a fresh wound at the time of primary debridement,[12] or at the time of early reparative closure of the wound, as described by Churchill.[2] When this is done, continued retraction of the divided nerve ends is prevented, and ultimate re-exposure of the separated stumps will be simplified at the final repair. For this purpose we have used slightly heavier (0.005″) sutures and have left one end of the tie long and protruding out to the subcutaneous fascial layer. On re-exploration it is then a very simple matter to palpate the metallic tip as soon as the skin has been laid open, and to follow this guide down to the point of nerve injury.

PREVENTION OF REFORMATION OF EXCISED NEUROMATA

Although Boldrey's[1] suggestion of drawing the nerve from which a painful neuroma has been removed through a tunnel drilled in a neighboring bone has been a partial answer to the problem of preventing their recurrence, there are many occasions when this procedure requires a considerable enlargement of the incision and unnecessary operative trauma. A simple snugly-fitting cap of sheet tantalum appears to answer the purpose equally well and requires no larger exposure than is necessary for the excision of the

FIG. 6. X-ray to show tantalum cap in position after resection of painful amputation neuroma from digital nerve. The relief of local tenderness was effective over an observation period of four months.

neuroma. This convenient device was developed by Colonel Spurling at the Walter Reed General Hospital, where it has since been found effective by Lt. Colonel Woodhall, as it has been also at the U. S. Naval Hospital in Chelsea. The technical steps of its application are illustrated in Fig. 5 and an x-ray of such a cap in position is reproduced in Fig. 6. Relief of local hyperaesthesia and tenderness at the nerve ending has given clinical evidence of success on numerous occasions, while direct inspection after reopening the incision has been carried out by Lt. Colonel Woodhall[14] and by us, demonstrating effective prevention of end-bulb reformation. It is important not to

apply such a tantalum cap when the nerve end lies so close to the skin that the patient may notice a subcutaneous mass. In this situation, which is the case in painful neuromata of digital nerves, Boldrey's procedure is preferable.

PREVENTION OF REGENERATION OF CENTRAL CONNECTIONS OF DECENTRALIZED UPPER THORACIC GANGLIA IN PREGANGLIONIC SYMPATHECTOMY OF UPPER EXTREMITY

When this operation through a posterior third rib approach was described by Smithwick,[8] he recommended covering the second and third thoracic

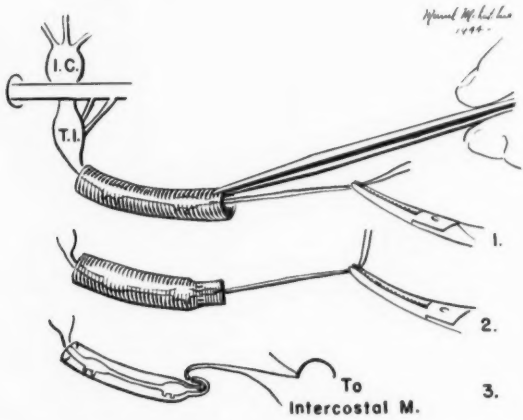

FIG. 7. Application of tantalum cap to decentralized upper thoracic sympathetic ganglia to prevent re-connection with regenerating preganglionic fibres. (1) After the sympathetic chain has been divided below the third thoracic ganglion and its central connections with the second and third thoracic anterior roots have been divided, the tantalum sleeve is slipped over the mobilized cephalic stump. (2) The open end of the sleeve is crushed and then (3) bent back on itself and crushed again. (Compare with Fig. 71, p. 408, White, J. C., and Smithwick, R. H., *The autonomic nervous system*. New York: The Macmillan Co., 1941, 2nd ed.)

sympathetic ganglia with a closed sleeve of fine silk gauze. The purpose of this manoeuvre was to prevent regeneration, which frequently occurred even when these ganglia were transplanted out of their normal bed and sutured to the second intercostal muscle. Regenerating fibres from the fourth thoracic ganglion or from the central stumps of the second and third intercostal nerves were apparently able to bridge this gap. The substitution of a tantalum sleeve, closing its lower end by crushing in a haemostat (Fig. 7), has simplified this step and should prevent the regrowth of preganglionic vasoconstrictor fibres even more effectively. On theoretical grounds, there should be less fibrosis and destruction of the two ganglia that are enclosed within the sleeve. These structures contain an appreciable number of postganglionic neurone cells, and it is therefore highly desirable that they should not degen-

erate and thereby sensitize the denervated brachial arterioles to circulating adrenaline and sympathin.[13]

DISCUSSION

Time alone can tell whether the application of metallic tantalum sleeves with closed ends can prevent reformation of neuromata or the regrowth of preganglionic connections with decentralized upper thoracic sympathetic ganglia. These procedures are being reported at this early date because of their technical simplicity and early promising results in the treatment of two common complications of peripheral nerve wounds—painful neuromata and vasomotor disturbances. It is desirable that these methods be given a wide trial and their value assessed by a number of independent observers.

The technical advantages of suturing severed nerves with tantalum wire rather than silk, and particularly the advisability of protecting the suture line with a tantalum sleeve have been questioned. In our opinion, the use of tantalum sutures has come to stay for the following reasons:

1. Tantalum causes less tissue reaction than silk.

2. Metallic sutures are safer to use than silk in the presence of potential infection. This is of particular importance in view of the recent trend to early reparative operations reported by Churchill.[2] An increasing number of gunshot injuries of nerves are being sutured or loosely approximated overseas under the protection of penicillin within a short interval of the time of wounding.

3. Metalllic suture material permits subsequent verification by x-ray that the approximated nerve ends remain in apposition.

The value of covering the area of nerve suture with a tantalum sleeve is less obvious, and proof that it results in better recovery of nerve function is still far from certain. No doubt better substitutes will become available, such as elastic films of collagen, which are just coming to clinical trial and which are gradually absorbed, but at present it appears that much may be gained by the use of tantalum sleeves under certain conditions encountered in the suture of peripheral nerves. The following points deserve comment:

1. Since a tantalum sleeve protects against ingrowth of scar tissue, less accurate approximation of the epineurium is necessary and fewer stitches are necessary to perform an anastomosis. Each additional suture injures a number of axis cylinders and leads to increased fibrosis at the line of anastomosis.

2. In a patient where the postoperative x-ray demonstrated a separation of the sutured nerve ends of the posterior tibial nerve over a centimeter in extent (Fig. 4), re-exploration on the thirty-fifth day demonstrated perfect gross reconstruction of the nerve within the sleeve of tantalum, and there has since been such perfect regeneration that this sailor has been able to return to active duty within six and a half months. This possibility has been suggested in the animal experiments reported by Weiss.[11] According to this same investigator, it also seems probable that the presence of a sleeve serves

to orient the down-growth of axones so that they cross the line of suture with minimal distortion.

3. Subsequent re-exploration with removal of the tantalum sleeve has invariably revealed a smooth, glistening reconstruction of the epineurium so that the exact point of suture has been hard to identify. This area is well supplied with blood vessels which run down from the proximal stump. The freedom from adhesions to surrounding tissues, when compared with nerves sutured without such protection, is striking. This is particularly true when the area of suture cannot be buried in a bed of muscle, but is exposed to the friction of adjacent tendons at the wrist, or contiguous bone where the peroneal nerve crosses the neck of the fibula, or where the radial nerve winds around the humerus.

One possible objection that has been raised to protecting an area of nerve anastomosis with any type of sleeve is the possibility that this portion of the trunk may be deprived of its blood supply. Tarlov and Epstein[10] have pointed out that, in addition to the longitudinal supply of blood vessels along a nerve trunk, there are frequent vascular twigs which join it from neighboring vessels. In a simple anastomosis cutting these off over a length of several centimeters cannot make the slightest difference, as the longitudinal circulation within the nerve is more than adequate to supply its ends. In the course of nerve grafting, however, any factor that reduces revascularization from the surrounding tissues may well impair the viabsility of the grafted segment. Here it would be highly probable that the ingrowth of vessels from the proximal and distal ends of the nerve would be too slow to prevent necrosis of the graft and its turning into a barrier of scar tissue. Davis[3] has very properly pointed out that "delaying the blood supply, even to a fresh graft, by surrounding the suture lines or the entire graft with metallic sheaths or tubes of any kind will only enhance the necrosis." The use of sleeves of any type in nerve grafting is therefore not advisable.

Another theoretical drawback to any metallic suture or wrapping is the possibility of dangerous heating if these areas are subsequently exposed to high frequency induced currents, such as are developed by some of the modern diathermy machines used in physiotherapy. This danger is, of course, no greater than that encountered after the use of other varieties of metal which are so commonly used by orthopaedic, plastic, and dental surgeons. The probability of injury from induced high temperature appears to be remote, otherwise frequent accidents should have already been reported. Pudenz has tested the effects of short-wave diathermy on tantalum and other metals in the tissues of experimental animals. In a preliminary investigation[6,a] he was unable to demonstrate any significant heating of the metal or evidence of thermal injury in the histological sections. In a more recent statement[6,b] he has reaffirmed his belief "that short-wave diathermy in therapeutic dosage will not heat metals to a degree that would be destructive to contiguous tissues." Nevertheless, experienced physiotherapists have always tried to avoid the risk of excessive heating induced by high frequency currents in

areas of the body containing metal. We therefore still feel that it is advisable to warn patients of this potential danger.

With these points in mind, it has become our practice to cover the area of nerve suture with a protective sleeve of fine sheet tantalum 1 to 2 cm. in length whenever it is impossible to bury the sutured nerve in a bed of uninjured muscle. This has now been carried out in a series of 22 cases. Such use of protective metal sleeves is not a fool-proof procedure, and requires certain very definite precautions. While sleeves of annealed tantalum 0.00075″ in thickness are not subject to crumpling and fragmentation, as was the case with the thinner foil that was first used,[7] they cannot be employed at a point of extreme flexion, such as where the median and ulnar nerves pass beneath the flexion crease at the wrist. Furthermore, they should not generally be employed unless the patient can be kept under continued observation by the surgeon who performed the operation and later progress observed. If the nerve fails to show clear-cut signs of regeneration in the minimal period to be expected, the area of suture is re-explored under local anaesthesia, the metal sleeve removed, and the sutured nerve tested by electrical stimulation for sensory and motor transmission. This has been carried out in only 7 of our 22 patients, all of whom have shown afferent transmission across the suture line and subsequent satisfactory recovery. There is one patient, however, in whom the application of the metallic sleeve may have been the cause of failure of regeneration of an ulnar nerve sutured at the wrist eight months ago. At two and one-half months after operation, when the patient was last seen prior to his transfer to another Naval Hospital, he had recovered sensation to pin-prick 2 cm. down his hypothenar eminence. As a result of his transfer he was not followed with sufficient care to make sure of a satisfactory recovery, and he was discharged from the service by Medical Survey at too early a date. In answer to a recent follow-up letter he has reported that he has had no further recovery. This single failure of a nerve to regenerate after an apparently satisfactory sleeve suture serves to emphasize the importance of keeping every case under personal observation until there has been a good recovery of function. Otherwise the use of these sleeves is not justified. In all the other cases, in which there has been an adequate period of observation, it has been our impression that these men have done as well as, or better than, those with simple suture in whom no sleeves were used. The following examples are quoted to bring out this point:

Kenneth C., Pfc. USMC. Five months prior to suture this marine had been struck by the empty metallic jacket of a Japanese 25-caliber bullet, which penetrated his forearm butt end first just below his elbow. The median nerve was completely divided and the surrounding flexor muscles of the forearm were severely traumatized by the disruptive effect of the defective bullet. On account of the excessive fibrosis the line of suture was protected by a sleeve of tantalum, which was removed nine weeks later. When discharged from the Marine Corps after eight and one-half months, anaesthesia of the palm and fingers had entirely disappeared. Although the tips of the first three fingers were still hypaesthetic, a trophic ulcer of the index finger tip had healed. There was good recovery of the flexor sublimis and opponens pollicis, with definite evidence of early reinnervation of the flexor pollicis longus and flexor profundus

muscles. Electrical skin resistance determinations showed that sympathetic axones had regenerated to the proximal phalanges.

George B., Lt. (jg), MC, USNR. This young medical officer had suffered a severe laceration over the anteromedial aspect of his wrist two months before. The lacerated tendons and ulnar artery had been dealt with satisfactorily at the primary debridement. After excision of a long fusiform neuroma and the contiguous fibrosed areas of the ulnar nerve, it was necessary to transplant its trunk in front of the elbow and free up its entire length in the forearm, in order to permit a suture without tension. The suture line was protected with a tantalum sleeve because it lay in contact with the tendons and considerable scar tissue. Sensory recovery was rapid and the patient could feel a pin-prick over the entire ulnar area within a period of five months. Now at eleven months there has been good recovery of light touch and vibratory sense. The points of two pins can be differentiated at 3 cm. on the palm and 2 cm. on the little finger. There is no visible atrophy of the hand, but this was less pronounced than usual at the beginning. He has strong adduction of his thumb, good interosseus power in the index and ring fingers, and some adduction of the little finger. Electrical skin resistance tests show practically complete recovery of the sympathetic axones. He has recently assisted us in performing other nerve sutures and has an excellent surgical hand.

Parker J., GM 3/c, USN. A month prior to the suture of his common peroneal nerve this sailor had been struck by a shell fragment over the head of his fibula, which had not completely severed the nerve but left it reduced to a narrow band of scar tissue 1.5 cm. in length. This area was excised, the freshened ends of nerve sutured with tantalum wire, and covered with a tantalum sleeve where the completed suture lay in contact with the neck of the fibula. The speed of sensory recovery down this man's leg is difficult to explain. At two months only two small islands of hypaesthesia, approximately 2 by 6 cm. in extent, remained just above the ankle and on the dorsum of his foot above the big toe. When last seen at three and one-half months only faint patches of hypaesthesia could be detected over these areas, and light touch was well perceived throughout. Two-point discrimination was normal above the ankle, and on the dorsum of the foot only twice that found in corresponding areas on the opposite side. Although the anterior tibial group of muscles had not yet recovered, there was fair power in the peronei, and electrical skin resistance determinations showed that sympathetic recovery was already complete.

SUMMARY

1. The use of fine wire and sheets of metallic tantalum are discussed in connection with both the repair and the prevention of regeneration of nerves. This element causes practically no reaction on the part of neighboring tissue cells, and it is now available in several forms of especial value in operations on peripheral nerves.

2. It is ideal for nerve suture, as it can be drawn to extreme thinness (0.003″), ties with ease, and can also be subsequently visualized in the x-ray as a marker of the position of the divided nerve ends.

3. In sheets 0.001″ thick it can be cut and rolled to fit the end of a nerve stump from which a painful neuroma has been removed. By crushing the distal open end a snugly fitting cap is formed which effectively prevents reformation of the neuroma.

4. The same procedure is recommended for sealing off the cephalic stump of the divided thoracic ganglionated chain in preganglionic sympathetic denervation of the upper extremity.

5. Annealed rolls of sheet tantalum (0.00075″) constitute a distinct improvement over the former use of foil in the protection of nerve anastomoses.

Unlike the finer foil, these sheets show no tendency to crumple or fragment, and their use is of real value under special circumstances which are often encountered in wartime injuries. Certain precautions are listed which are of great importance in their application.

The authors are indebted to Professor Paul Weiss of the University of Chicago for preparing the original supply of annealed sleeves of sheet tantalum, and to Dr. I. R. McCall of the Ethicon Suture Laboratories for generously furnishing a supply of all the above-mentioned tantalum products before they came into commercial production.

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HEMOSTASIS IN NEUROSURGERY

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"The confidence gradually acquired from masterfulness in controlling hemorrhage gives to the surgeon the calm which is so essential for clear thinking and orderly procedure at the operating table." Halsted

INTRODUCTION

THE PURPOSES of this article are two: first to list and evaluate the several devices employed by neurosurgery in the control of hemorrhage and, second, to show how neurosurgery has been led inevitably to utilize the clotting functions of blood itself as an aid to hemostasis and to interpret the more recent innovations by reference to those functions. In discussing the whole range of the hemostatic procedures of neurosurgery, a larger purpose is also thereby served, namely, to acquaint general surgery, and its other sub-branches, with the details of modern hemostasis without ligature. For it is a curious and inviting thought that the feature that most aptly distinguishes neurosurgery as a specialty is the control of hemorrhage without the use of the ligature. The delicate and pulpy nature of the central nervous system, the fineness and indispensability of its structures, the close confinement of the avenues of approach, and the relative depth at which work is done, all combine to make hemostasis with the ligature virtually an impossibility. It has fallen upon neurosurgery, therefore, to devise methods of bleeding control that are workable under the peculiar circumstances of its several fields of activity, with the result that an impressive catalogue of methods has grown up during the three-score years by which neurosurgery counts its age, each one in turn resulting in a drop in the mortality rates, a strengthening of surgical courage, and a shortening of the time consumed by an operation.

It is a mistake, however, to presume that the principle of hemostasis without ligature is modern in origin. On the contrary we have but reverted to the practices of the ancients and in a sense have regressed from the pinnacle to which, after a long struggle, surgery rose when in 1876 Lister introduced the chromicized catgut suture and Halsted in 1879 turned the use of that ligature into a delicate and discriminative procedure by inventing the modern hemostat. One of the "musts" of any surgeon's library is the attractive little book, *The History of Hemostasis*, by Samuel C. Harvey (1929),[27] which acquaints us with the story of the control of bleeding from the earliest recorded medical times until the turn of the present century. It will be found there that many of the methods described in this paper are but refinements of practices employed during that incredibly long journey by which our scientific ancestors progressed toward the final adoption of the principle of ligation of vessels.

This study is concerned only with methods for accomplishing permanent hemostasis, not with the temporary control of bleeding during the course of an operation.

HEMOSTATIC METHODS

1. BONE WAX

It is altogether fitting that the introduction of bone wax to surgery should have been accomplished in a laboratory experiment by Victor Horsley while he was preparing for his career in neurosurgery (1885), prior to his appointment at Queen Square, prior even to the first of those ten initial intracranial operations[30] by which he established both his fame and the essential hopefulness of brain surgery. A little note in the *British Medical Journal* for 1892,[31] written in response to an inquiry, recalls the event. Some technique of Magendie had given him the idea, and he tried modelling wax worked soft in the fingers on the free bleeding cut surface of the cranial bones in dogs. As such a proceeding instantly arrested the bleeding, he attempted to make an antiseptic compound for operations on man, which, however, was not satisfactory. He then enlisted the aid of a Mr. P. W. Squire to make experiments so as to arrive nearly at the tenacity of modelling wax, and in this he succeeded with the following formula: beeswax, 7 parts; almond oil, 1 part; salicylic acid, 1 per cent. Horsley added that it is nearly always sterilized by boiling before use, and kept in covered stoppered bottles.

2. THE CUSHING CLIP

"The thought has doubtless occurred to many that much time and trouble would be saved in major operations could there be devised some form of haemostatic clamp, the mere placement of which would leave a fine, knotted ligature on the bleeding point so as to obviate the alternatives which we now possess, either of leaving a pendent instrument or taking the time necessary for ligation."

Thus wrote Cushing[11] in 1911, by way of introducing the tiny implantable metal clip that has come to bear his name. Improvements there have been in manipulation of sutures and ligatures, including a simple form of the Singer sewing machine, but thus far nothing has appeared that produces a knotted ligature without digital effort, and the Cushing clip meanwhile has been put to an increasing number of uses "in operations during which vessels are necessarily divided at depths easily reached by a clamp but in positions awkward for ligation," and it now does real service in the thoracic and retroperitoneal spaces, in addition to its primary domain of the brain and spinal cord. Whereas, however, the metal clip had formerly to be used upon vessels of all sizes, and consequently in large numbers, it is now possible to coagulate the smaller vessels with the electric cautery and reserve the use of the clip to the occasional larger artery or vein, with consequent reduction of the numbers of implanted metallic "ligatures" and a noticeable improvement in the radiographs taken subsequent to operation, if not for any demonstrable physiological gain. Further inroads upon the use of the metal clip are

imminent with the opportunity to halt bleeding from veins by the application of an absorbable matrix soaked in thrombin, so that the clip may soon be reserved for occlusion of small to medium-sized arteries, notably the middle meningeal and the several confluents and branches of the circle of Willis, not excluding the intracranial portion of the internal carotid.[16] General surgeons, and those of the other specialties, would do well to study the possibilities of the metallic ligature in connection with similar situations in their work.

The original Cushing clip was hand-wrought by an ingenious method. The silver wire was wrapped tightly about a rod which bore sharp flutings, and grooves in its opposite sides. The several turns of the wire were hammered against the flutings to produce transverse ridges, and individual clips were then cut apart by means of scissors sliding along the grooves. Thus the clips bore a fine ridging which helped prevent them from slipping off after being squeezed shut upon the vessels. Clips are now fabricated by a tool which cuts, shapes, and embosses them at a single operation, but in other respects the original invention stands fundamentally unchanged in the newer models: a rack for storage of the prepared clips; and a carrier with grooved nosepiece and a spring-and-rachet handle, to serve them up to the surgeon's use. A recent innovation has been the substitution of inert tantalum for the more erodable silver wire, a refinement of some importance. A possible further addition of value would be the production by instrument makers of an alternate size, one moderately larger than the present standard to bring within its scope vessels that cannot be fully secured by the present clips yet are not too large to be held safely within the jaws of a crimped wire.

3. ELECTROCOAGULATION

Cautery with the hot iron was used to some extent in Hippocratic times and it became the paramount tool of the surgeon, to the point that it replaced the knife, in the degraded medicine of the middle ages—"any one could apply the cautery, practically no one the ligature," remarks Harvey. Selective use of the cautery to sear an artery and promote tight coagulation of its edges was recommended by Albucasis (11th century). It was the achievement of Paré (1552) to make clear the great advantage of the ligature over the cautery, yet surgeons were loath to relinquish a practice that derived authoritative support from Hippocrates and Galen, and about which had grown up a huge ritual, so that two hundred years later the cautery was still in spotty use. Ultimately it died out to await rejuvenation in the guise of electrosurgery.

The discovery by d'Arsonval (1891)[1] that electrical currents of high frequency alternation are devoid of the physiological stimulation (muscle twitching and pain) long known to be associated with the low frequencies used in power transmission, set the stage for the twin fields of medical diathermy and electrosurgery, as these branches came to be called. The basic effect employed by both is that of heating. In diathermy the heating energy

is diffused over a large area and the resulting rise of tissue temperature is slight and within physiological limits. In electrosurgery the current, and consequently the heat, is focussed at the end of a sharp-pointed or other small terminal electrode, causing necrobiotic effects varying from slight dehydration (desiccation) up to the point of boiling and coagulating the tissue proteins in their own juices, or of outright charring. Extraordinary tissue temperatures are sometimes reached in electrosurgery; it was shown by Doyen[17] that the spark from an electrode held a short distance away from the tissue produces temperatures in the carbonized area as high as 1,100°F. (heated iron as used in medieval times turns to light yellow at 400°, purple at 550°, dull red at 1,000° and cherry red at 1,600°F.). When, however, the electrode is placed in direct contact with the tissue the concentrated heating effect of the arc is lost, and tissue temperatures, as measured by Doyen, confirmed subsequently by Ward and West,[40] and again by Huntoon[36] appear to lie in the zone 150°F. to 180°F. Electrosurgery then, when used correctly, can be held down to the range of simple protein coagulation, although few of us lay claim to completely avoiding the "popping" that occurs when steam is generated or the charring at still higher temperatures from the spark discharge.

In view of the critical dependence of neurosurgery upon methods of hemostasis that do not involve implacing and tying a ligature, it is difficult now to explain the long delay of that specialty to investigate and adopt what has become the number one device in the list. The d'Arsonval apparatus was used for destruction of skin lesions by Rivière[51] as early as 1900, and Doyen[17] in 1907 supplied the important improvement of a large indifferent "ground" plate. By altering the design of the circuit, W. L. Clark[6] in 1910 obtained what proved microscopically to be tissue dehydration, and for this mild type of electrosurgery he proposed the term desiccation. Clark also added considerably to the power and quality of the instrument by installing multiple spark gaps in the place of the single gap then in vogue. Meanwhile Lee deForest, in 1908, using his newly invented 3-electrode thermionic valve, had supplied the first radio tube high frequency apparatus capable of furnishing a cutting current, with which Neil and Steinberger, experimenting on dogs, "made fine, clean incisions with little bleeding."[40] That this was not an isolated example of the use of electrosurgery in the role of the scalpel, is revealed by two reports issued in Europe in 1910[14,20] describing electrical methods of cutting tissue. Finally, the tuned frequency of the circuit was increased from the 500,000 cycles common to the diathermy apparatus, to the more effective 2,000,000 to 3,000,000 cycles of electrosurgery not, as Cushing[12] remarks, by Bovie in 1926, but by Doyen in 1907–1908.[17] Thus the essential features of electrosurgery as we know it today were all at hand by the end of the year 1910, including the choice between the multiple spark gap machine and the vacuum tube oscillator, the determination of the most suitable frequency, and a knowledge of the effect of electrical heating upon tissues, including the terms *fulguration*, *coagulation*,

desiccation or *dehydration* and *cutting current*. It is true of course that one could scarcely thumb through a catalogue and order a "Burdick" or a "Bovie" but the experimentive surgeon of the day could and did find equipment builders who produced passable models for his use. It is a matter of record that electrosurgery was early extended from the lesions of the skin to internal surgical fields, being adapted to hemorrhoids in 1907,[8] the tumors of the bladder in 1910[3] and by its outstanding advocate, W. L. Clark,[6] to a large variety of applications, including the breast, cervix, tongue and throat, being found especially useful in the highly vascular structure of the angiomata.

Thus it is scarcely creditable to neurosurgical acumen that it was not until 1926 that the accidental proximity of an electrophysicist working in a cancer hospital on one side of Van Dyke Street in Boston, and a pioneer neurosurgeon on the other, brought about the long awaited trial of electrosurgery in what was to be its most perfect application, hemostasis in the field of brain surgery. We owe deep gratitude to Cushing for the energy with which he adopted this idea once it came to mind.*

> When I first had the good fortune to see this [electrosurgical] loop being used bloodlessly to scoop out bits of tissue from a malignant tumour for purposes of biopsy, I foresaw that a new tool had been put into our hands to facilitate the piecemeal removal of at least some of the heretofore inaccessible intracranial tumours.[12]

He proceeded to try out electrosurgery first upon cranial tumors, then upon neoplasms of the intracranial chamber. With its help, he succeeded in doing at a single stage what previously had required two or three separate operative procedures, and so taken was he with the result that he made one case (an olfactory groove meningioma) the subject of his *MacEwen Memorial Lecture* delivered in Glasgow in 1927.[12] Next year he reported (with Bovie)[13] on the use of electrosurgery in some five hundred odd operations, and mentioned details of technique, especially the importance of applying the cautery precisely upon the bleeding vessel (which would have pleased Albucasis), according to the maneuver introduced earlier by Ward[62] of grasping the vessel walls between the points of the dissecting forceps (or a hemostat) and conducting the current from a contact made upon the handle. He foretold the gradual recession of the silver clip from its paramount position in neuro-

* The following anecdote has come by letter from Dr. S. C. Harvey: "John Morton and I were attending a session of the American Medical Association in Atlantic City in June, 1925 and were watching a demonstration of the use of a desiccating and cutting diathermy machine on a big block of beef, such as is regrettably unobtainable these days! Dr. Cushing came along, stopped to speak to us, and in a purely jocular fashion, one of us, I am not sure which, said, "Here's something you ought to use on the brain!" Not that we had any idea it was applicable there, but I think with the mischievous purpose of stirring Cushing up at the thought of employing such a gross and disgusting procedure as was evidenced in the demonstration. We did not get the reaction we expected from him. He seemed rather thoughtful, and we separated after a time, with no further thought about the incident. He apparently returned to Boston, and being aware that they were trying out Clark's method of removing malignancies at the Huntington, established contact there. Bovie of course was the physicist, and was working at the time on improving the high frequency apparatus and was in the process of developing a better machine than had been manufactured before. It may have been that Cushing had this in the works before he went to Atlantic City, but he gave no evidence of it at the time, and I cite it as evidence—scarcely necessary —of his alertness and aggressiveness in picking up a new idea."

surgery, since, "though for the control of the larger vessels clips cannot be wholly superseded, they are used less and less frequently and the current more and more for hemostasis."

Thereupon electrosurgery spread throughout the specialty, receiving notice from Sachs[52] and, with certain warnings, from Dandy.[15] It is eminently useful in disposing of veins, especially the free-lying veins that bridge the subdural space between the brain and the dural sinuses. Small arteries also can be treated with dispatch, although with some electrocautery fails unless assisted by a clip. Many surgeons sear a pathway into bloodlessness before incising the cortex. A few minor improvements in equipment have appeared: the attachment of the conducting wire to a terminal on the (metal) suction tip[28] proves to be a convenience when surgical teams are shorthanded; and the introduction of forceps with mutually insulated points facilitates concentration of the current flow upon the tissue held between them (theoretically a refinement upon Ward's suggestion; in practice, somewhat cumbersome). Both spark gap machines and those based upon the vacuum tube are purchasable, and superb results are possible with either class of equipment if the operator will but learn how to get the most from it.

4. STYPTICS

The styptic (having the power of contracting organic tissue; that which arrests hemorrhage; astringent.—*Oxford English Dictionary*) was never a hemostatic of good choice in surgery. Invariably it was a substitute, an improvisation, which succeeded or not according to luck as well as the skill and patience of the surgeon. It comes down to us from antiquity, having received mention from Galen and the medieval chroniclers, who left rules for implanting the alum, the copper sulfate button, or the ferric chloride granules against the vessels of the amputation stump.

While the styptic is intended to be localized at the point of bleeding, in practice its caustic action includes the neighboring tissue, be that muscle, fat, mucous membrane or what not, and the ultimate control of hemorrhage depends upon a lifeless eschar which covers and confines the bleeding vessel. The precipitation of proteins caused by the action of the chemical is not that highly specialized crystallization of fibrinogen into fibrin by which nature coagulates blood, but an indiscriminate amorphous destruction of all protein elements. As a hemostat, the resulting eschar is poor in quality and unreliable. Except to complete the list of agents employed by neurosurgery, the styptic could be put aside as unworthy of mention in the face of its modern rivals of the biochemical series. In times past, however, neurosurgeons have often deliberately impressed powerful caustics to the task of hemostasis. For example, it was Cushing's habit in later years to have at hand on the instrument tray a basin of Zenker's solution (corrosive sublimate 5 parts, potassium bichromate 2.5 parts, sodium sulfate 1 part, water q.s. 100), partly for destruction of neoplastic remnants following tumor extirpation, but partly also to use in daubing upon bleeding spots that failed to re-

spond to other treatment. This practice he began while doing the transsphenoidal operations upon adenomata of the pituitary (the thrombin-soaked patch was not yet born), and found it useful also after evisceration of acoustic neurinomata.* I had a brief moment of glory upon my first day of service at the Brigham Hospital when by accident I upset the entire contents of this basin into the wound.

DISCUSSION OF THE FACTORS INVOLVED IN THE BLOOD CLOTTING MECHANISM AND THEIR UTILIZATION IN SURGICAL HEMOSTASIS

Before continuing to the remaining sections of this review, it will be helpful to examine briefly the physiology of the coagulation of the blood.†

Fibrin, the end result of the biochemical action by which blood clots, is the meshwork that springs into existence to trap and freeze the corpuscles and prevent their further flow. All of the constituents of fibrin are present in normally flowing blood. The trigger that releases these constituents, the chemical forces that drive them into the chain of combinations resulting in the clot, and the true nature of the constituents themselves, have formed the waters of an immense sea of investigation which as yet are by no means thoroughly fathomed. Surgeons, and in particular neurosurgeons, have followed the charting of these waters with avid interest, hoping that by some magic there would appear a device to ease the task of blood stopping and so shorten their labors, and it is important to observe that from the earliest days of neurosurgery one or another segment of the blood clotting mechanism has been employed, with varying degrees of success, in the hemostasis of capillary ooze and venous bleeding. To understand the action of these hemostatic aids one needs to familiarize himself once again with the equations representing the coagulation of the blood, which were introduced forty years ago and are still considered correct.

I. Prothrombin + Ca^{++} + thromboplastin = thrombin.

II. Fibrinogen + thrombin = fibrin.

It will be noted that four parent substances are involved, each of which deserves brief discussion. *Prothrombin*, the precursor or mother substance of thrombin, is a constituent of plasma as well as of lymph, and is distinctly an extracellular substance. Its presence in the blood depends upon a normally functioning liver and upon an ample supply of vitamin K, so that a hemorrhagic diathesis can be expected in disorders involving obstructive jaundice, biliary fistula or liver damage. *Calcium* is indispensable to the coagulation process, and the simple displacement of calcium by a citrate or an oxalate prevents the reaction from taking place. *Thromboplastin* is the trigger that discharges the mechanism. In contrast to prothrombin, it is an intracellular substance, and this physical separation of the two serves to hold the coagulation process in check until by injury, or by some artificial stimulus, their

* Letter from S. C. Harvey.

† Condensed in large part from A. J. Quick: *The Hemorrhagic Diseases and the Physiology of Hemostasis.*[50]

chemical combination takes place. In the circulating blood, thromboplastin is carried almost exclusively by the platelets, to be released when they agglutinate; the disease hemophilia is based upon a deficiency of platelet thromboplastin or a disorder of platelet behavior which tremendously hampers the supply of this essential element. Thromboplastin is also found, intracellularly, in most other tissues of the body, notable amounts being present in the brain and the lung.

The successful combination of these three elements, prothrombin, calcium and thromboplastin, leads to the formation of an intermediary product, thrombin. It remains now to combine thrombin with fibrinogen to form fibrin, the end product of the clot. *Fibrinogen*, a plasma protein, possesses one unique characteristic that differentiates it sharply from its two companion proteins, serum albumin and serum globulin; it is converted by the action of thrombin from a colloidal sol to a gel which microscopically shows a crystalline-like structure. This ready conversion to an insoluble compound makes it an ideal hemostatic agent in nature. By good fortune, too, the supply of fibrinogen is rarely if ever at fault, and the amount in the blood is at least five times greater than is needed for the effective control of hemorrhage.

From this very brief examination of the coagulation process it becomes apparent that the strategic point of attack, for purposes of surgical hemostasis, is the addition of *an active prepared thrombin* to the flowing blood at the point of its emission. Two good reasons dictate this choice rather than any other. First, the occasional defects of the clotting mechanism lie almost exclusively in the preliminary steps by which thrombin is formed, and such defects (hemophilia, jaundice, etc.) are thus circumvented if the first reaction is by-passed. Second, the reaction between thrombin and fibrinogen is the last step in the process, and it goes forward with considerably more force and speed than does the reaction to an artificial stimulus applied to the initial stages. Only recently, however, has this choice become evident or, indeed, practical, and neurosurgical progress in biochemical hemostasis, as one might designate this tool, was long concerned with substances containing thromboplastin, with end products which bear traces of the primary factors, or with rough-textured substances tending to agglutinate the platelets. The story begins with the simplest form of hemostasis, natural clotting, and takes up in succession the methods by which the natural process can be speeded up.

5. PATIENCE AND PRESSURE

One of the basic ingredients of neurosurgery is patience, or at least so it has been until very recent times, and in the era of the 6, 7, and 8 hour operations for brain tumors a great deal of the time spent, while the surgeon and his weary team shifted collectively from one foot to the other, was consumed in fact by a succession of experiments in the normal clotting time of blood. Five to 8 minutes is the average space of time for a good clot to form, and if the clot attaches itself with sufficient firmness, and provided that the

after-coming pressure is not too great, the flow of blood is effectively checked by nature.

A small increase in the magnitude of the hemorrhage alters the situation. Then the volume of flow or the backing-up of pressure washes away the precipitating clots as fast as they form, leaving nothing to plug the rent in the vessel. But natural clotting will bring even these hemorrhages under control if a little pressure is applied to hold the vessel walls together and give the clot time to solidify and adhere before it is called upon to assume the responsibilities of a hemostatic, and such temporary compression of vessels during thrombus formation is probably the oldest method known in the control of hemorrhage.[27] Moreover, it is thoroughly practical in many situations today, especially if the compression can be maintained without attention from the surgeon who goes about other phases of the operation while awaiting the formation of the clot. A suggestion made by Grey,[24] which has been revived and put to highly effective use by Poppen,[47] is the laying down of a piece of rubber tissue (gutta-percha) against the bleeding vessel before applying the cotton pledget. This is done to prevent adherence of the clot to the material, since ordinarily the smooth rubber surface can be peeled away without disturbing the clot.

6. ABSORBABLE PACKS

It is but a short step from the temporary pressure which results in a permanent clot to the use of a soluble or absorbable pack which can be left in place to await later resolution by the body. One such substance, oxidized cellulose, was introduced recently by Yackel and Kenyon[68] of the Eastman Research Laboratories and is supplied (thus far, only for research purposes) by Parke, Davis & Company. It is prepared from ordinary gauze sponges or cotton pledgets by the action of nitrogen dioxide, which converts certain of the hydroxyl radicals of cellulose to carboxyl groups, thus making the material soluble at the alkalinity present in tissue juices, while maintaining the original texture of the substance. Actually the cellulose in the form of cotton or gauze is converted into a solid organic acid with maintenance of its original structure and having a tensile strength of about two-thirds that of the original fabric. This product, because of its carboxyl content or acidic nature, is slightly hemostatic (in the manner of a styptic).

Because of its acidity (about pH 4.0) oxidized cellulose inactivates thrombin. This characteristic was not sufficiently understood during the early surgical investigation of the material. The error is apparent in the report by Putnam,[48] and accounts probably for the wide discrepancy in the clotting effectiveness of the same thrombins when tested *in vitro* upon fibrin foam and oxidized cellulose, as reported by Bering.[4] It was not until Seegers and Doub[55] (May, 1944) measured this inactivation experimentally, and showed the rate at which it proceeds, that the process was made clear. They supplied instructions for neutralizing oxidized cellulose at the operating table by dipping it in a 1 per cent solution of sodium bicarbonate, and this procedure was followed by Uihlein, Clagett and Osterberg,[60] whose re-

port constitutes the only reliable evidence thus far available on the utility of cellulose as a carrier for thrombin. It is a favorable report, but details are lacking, especially upon the important distinction between its functions as a pack and as an adhesive patch for soft yielding surfaces.

Inasmuch as aids to surgery tend to become rapidly specialized, it is a fair guess that oxidized cellulose with its palpable, incompressible, slightly styptic bulk will find extensive use in closed wound packing, while the fluffy, compressible, inert, sponge-like matrices (fibrin foam and gelatin sponge), serving as vehicles for thrombin, will be chosen where pressure packing is impractical because of the absence of rigid structures to support and confine the pack or inadvisable in proximity to such vital organs as the neuroaxis. Neurosurgery has few opportunities for pressure packing and a wide demand for hemostasis on soft unresisting surfaces, while the surgery of the extremities and other closed-wall locations often calls for hemostasis by pressure, and in these situations absorbable packs may become a very important aid. Oxidized cellulose is new, and still undergoing experimental and clinical investigation, and the reader is urged to refer directly to the investigators' reports.[10,21,22,23,48,60,61]

7. HOT WATER

The use of hot water irrigations for hemostasis is a matter of such common knowledge that it has proved difficult to trace the practice back to its point of innovation. For our purposes it may be said to begin with a paper read by the obstetrician Milne Murray[45] before the Edinburgh Obstetrical Society in the year 1886. At that time strong rivalries had developed between the advocates of cold irrigations and those of hot, both sides admitting that cold irrigations cause spasm of blood vessels and allaying of hemorrhage, but with one school maintaining that warmth of all degrees dilates vessels and promotes hemorrhage while the other, admitting readily the undesired effect of a bath of tepid water on an incised and bleeding wound, insisted that a stream of *hot* water directed on a bleeding surface, such as that exposed during an operation for vesico-vaginal fistula or for repair of the perineum, at once arrests hemorrhage by stimulating contraction of blood vessels. Murray put the proposition to the test in a well-executed experiment upon the uterine vascular network of rabbits, and two of his experiments deserve recounting here.

> In the first one, water at 40°F. was directed upon the vascular mesometrium stretching from the vagina to the cornua of the uterus on one side, while water at 115°F. was similarly directed upon the other. Four minutes was the duration of irrigation. Soon after the commencement of the stream, both sides became pale—almost white. At the end of four minutes the side receiving the cold water showed signs of returning vascularity, whereas that receiving the hot was still perfectly anemic. Four minutes later the cold side was bright red, the hot side was still white. Eight minutes after, the cold side was an intense scarlet, the blood vessels standing out in spiral lines all over the tissue, while the hot side had assumed the appearance it had before the experiment. Half an hour later the conditions were still the same.

This showed clearly, said Murray, that while contraction follows at once in

both cases, the contraction induced by the cold water is succeeded by an intense reaction, whereas the vessels constricted by hot water regain their ordinary tone slowly, and without reactionary congestion.

The second experiment concerned hemostasis. A pregnant uterus was incised, and the edges of the wound caught by a pair of hooks so as to hold them apart, and permit bleeding to occur. The blood escaped freely. A small stream of water at 123°F. was allowed to flow on the wound, when the bleeding immediately ceased. Cold water was gradually added to the vessel containing the water, and the temperature slowly fell to 100°F. About one minute afterwards the bleeding recommenced, at first slowly, but as the temperature fell to 90° the blood escaped more rapidly. During the five or six minutes which were necessary to reduce the temperature to 50°F. the blood continued to flow as before. When 46°F. was reached the escape of blood became markedly less, and, a piece of ice being added, the temperature rapidly fell to 38°F., and then to 36°F., when the bleeding entirely ceased, the water running off colorless. In about two minutes thereafter, the stream of water still being kept up, the oozing again commenced. A morsel of ice laid on the wound was quickly dissolved, and washed away in the escaping blood, and it was evident that the cold had lost its influence. The experiment was concluded by dipping a sponge in water just hot enough to be barely tolerable to the hand (115° to 120°F.) and wrung out over the wound when bleeding ceased. The incision was then closed.

Now it so happened that a Dr. Horsley, who we may presume was the young Victor, then 28, was present in the audience, and arose at the conclusion of the paper to ask a question (to which he received no answer). Evidently he took to heart the lessons of this demonstration, for he referred to it in detail in his address "On the Technique of Operations on the Central Nervous System"[32] in 1906, quoting Murray, whom I also quote:

It is certain that water from 70°F. to 103° or 105°F. will invariably dilate blood vessels and promote the flow from open ones, but it is equally certain that water of temperatures from 110°F. to 120°F. will have just the opposite effect.

Horsley found this to be correct in practice, and stated that what we require is a temperature that stimulates contraction of small vessels without at the same time causing heat coagulation of the nervous tissue. He felt that the temperature should not exceed 115°F. nor fall below 110°F.

Cushing therefore appears to have been on weak ground when in 1911[11] he advocated the use of solutions in the temperature range of 100° to 105°F. in his list of hemostatic aids but, so far as I am aware, he deviated little from this practice in later years, despite the tedious delays that often took place before tumor beds could be made dry.

Two questions remain to be discussed. Does an irrigation with hot water merely delay bleeding through temporary vasoconstriction, or does it produce permanent and true hemostasis? Second, what is the upper limit of temperature that can be safely employed without damaging nerve cells?

The answer to the first appears to be favorable to the hot irrigation. Howell[35] states that "hot sponges or cloths applied to a wound hasten clotting, probably by accelerating the formation of thrombin and the chemical changes of clotting," and Wiggers[65] agrees that heat "tends to accelerate all chemical reactions concerned in coagulation." Presumably,

then, hot irrigations promote both temporary vasoconstriction (of no little usefulness during the advance through tissue that is ultimately to be removed) and the coagulation of blood. Murray's second experiment, however, contains a note of warning with respect to the ability of heat to coagulate, because upon cooling it may be found that a portion of the control was of the nature of vasoconstriction and therefore temporary. The surgeon is best advised to use heat for what it is worth, preferably not during the last 10 to 15 minutes that the full field is exposed, unless followed by some supplemental step, such as laying tissues back upon each other to maintain vascular pressure.

The second question can be answered in part, but not with full satisfaction. Dusser de Barenne and Zimmerman,[18] using a carefully controlled heating element, charted the depths of destruction of the cerebral cortex in the monkey under the effect of temperatures ranging from 122°F. to 176°F., with exposure times of from $\frac{1}{2}$ to 5 minutes. From this we learn that an exposure of $\frac{1}{2}$ minute at a temperature of 122°F. resulted in death of nerve cells of the most superficial cortical layers. What degree of temperature the cortex (or indeed any structural part of the nervous system) can withstand *without* damage is not indicated, and it would be immensely valuable to neurosurgery if the Yale group would set up Dusser de Barenne's apparatus and make that determination.

Evidence from another source is helpful here. The work of Pincus and Fischer,[46] in a study of the thermal death point of cells grown in culture, indicates that a rise of 10°C. (18°F.) maintained for 30 minutes has no apparent effect and that a temperature of 13°C. (23.4°F.) above normal can be withstood for 2 or 3 minutes with growth inhibition but without death. Huntoon[36] concludes that an estimate of 11°C. above normal (for humans, this means a temperature of 118.6°F.) is quite conservative. Meanwhile therefore, until the problem is worked out specifically for the primate nervous system, it appears safe and reasonable to follow Horsley's advice, and keep the irrigating fluids between 110° and 115°F.

8. THROMBOPLASTIN

It may well have been that the abundant presence of a phospholipid coagulant in the cells of the brain played a major role in setting brain surgery upon its feet, and that nature in a measure made up for what neurosurgery lacked in its early days. This possibility was recognized by Horsley after his first few operations (1886), when his alert mind borrowed a contemporary discovery of physiology. He wrote:[29]

> No doubt one additional reason why the hemorrhagic oozing so soon stops in a brain-wound is that clotting is induced early by the presence of the lecithin proteid compound which exists in quantity in the brain, and has been discovered by Dr. Wooldridge[67] to play a very important part in the process of coagulation.

Thus began the interest of neurosurgeons in the physiology of hemostasis, and the adoption of its several processes to surgical use.

The next step was many years in coming, but it descended logically from awareness of the coagulating properties of bits of living tissue. Horsley[33] on one side of the Atlantic, and Cushing[11] on the other, independently and at about the same time (1909–11), began to apply small stamps of freshly-cut muscle to areas of capillary and venous bleeding, with gratifying results. Both men recognized that other kinds of tissue could be used, and tried bits of fascia among other things, but returned to muscle as superior to all. Horsley then went on to experimental studies of muscle implants, demonstrating that when held against torn vessels until bleeding stops, they possess to a satisfactory degree the property of adhesion, and measured this adhesiveness upon living divided arteries, finding that it withstood blood pressures of 60 to 80 mm. Hg. He examined the zone of adherence microscopically and observed blood platelets and fibrin fibrils within a few minutes of commencing the preparation. Finally, he demonstrated that muscle loses its hemostatic properties after boiling—all very sound work in the field of hemostasis.

The active principle of the tissues that promotes clotting was demonstrated by Howell (1912)[34,50] to be another phospholipid, cephalin, not lecithin as reported by Wooldridge. He showed it to be thromboplastic in nature, similar in properties and action to the corresponding substance carried by the platelets of the blood. Since that time preparations of thromboplastin of one sort or another have been available and Cushing, in an experiment unreported but well-remembered (1929–30), employed cephalin to halt the oozing from brain or dura by applying it on thin sheets of cotton, only to rediscover that any clotting agent fails if the vehicle upon which it is applied must be removed. At the present time, preparations of thromboplastin, extracted from lung or from brain, are marketed by several concerns, but their clinical usefulness is directed to the standard laboratory test for estimating the prothrombin concentration of the blood. Thromboplastin in all its forms, including the muscle implant, is rapidly being superseded by a much more active agent of hemostasis, thrombin, applied with an absorbable vehicle.

9. THROMBIN

"The action of thrombin in converting soluble fibrinogen into insoluble fibrin can be considered the most fundamental reaction in the coagulation of the blood."[50] This sentence from Quick tersely expresses the importance of the material upon which hopes are now pinned in the search for a rapid stimulus to blood coagulation in the operative field.

Thrombin has not yet been prepared in pure form. The relative purity was advanced by slow stages following the preparation available to Schmidt (who gave it its name) in the 1890's, until Mellanby[44] in 1933 produced a material with a potency of from 60 to 100 Iowa units* per mg. Further

* Defined (1938)[54] in these terms: 1 unit of thrombin is that amount which will clot 1 cc. of a standard fibrinogen solution in 15 seconds.

purification was not far distant. In 1938 a group (Seegers, Brinkhous, Smith and Warner)[54] at the University of Iowa succeeded in preparing from beef plasma a dried thrombin with a potency in the neighborhood of 300 to 500 units per mg., roughly 5 times stronger than Mellanby's product. When dissolved as a 1 per cent solution, 1 cc. of this material clotted 1 cc. of blood within 2 seconds. Here then, was a hemostatic substance of remarkable power. Its effectiveness was determined in animal studies[57] by applying the thrombin to bleeding surfaces with an atomizing spray. Two conclusions were reached: the material was non-toxic when so used; and it was reasonably effective in controlling ooze. The evidence of this preliminary report was then strengthened by studies[63] in which the toxicity experiments were extended to include intramuscular and intraperitoneal injections (6,000 units, in the rat) with no untoward effects and, sterility problems having been overcome meanwhile, trials were reported in 21 human cases. Successful hemostasis was accomplished in a case of mastoidectomy, in the donor area of a skin graft, and in the tooth sockets of hemophiliac patients still bleeding 24 hours after extraction. By 1940 the potency of their preparation was doubled[53] and it moved upward another notch in 1942,[56] by which time 1 mg. represented better than 1,500 units and contained less than 10 per cent of inert material. Extensive clinical experiences using this relatively pure product (thereafter marketed by Parke, Davis & Company) were reported by the Iowa investigators for 225 cases,[59] again through the use of a spray or wash or of the dried powder itself, but without employing a vehicle or tampon. Notable results were obtained, although secure hemostasis did not always follow because of the tendency for the clotted blood to float away under the force of aftercoming hemorrhage. Important findings were: the compatibility of thrombin with the sulfonamide group of drugs; the absence of local irritation; and the lack of sensitization in patients in whom the preparation was used repeatedly. In none of the cases was there evidence of intravascular thrombus formation. Beef thrombin, then, appeared to be not only a highly active clotting agent for human blood but, upon the evidence at hand, harmless in application.

Meanwhile, thrombin prepared from rabbit plasma had been tested on small experimental human wounds,[43] where it too served successfully to control bleeding.

A third source of thrombin was soon to be exploited. In a discussion of the physical chemistry of the plasma proteins, Cohn (1941)[7] suggested that human albumin could be prepared by the procedures then applied to obtain bovine albumin, and should prove useful for a number of therapeutic purposes, particularly in the treatment of shock due to acute loss of blood. No suggestion was ever more ripe for the times. The bloody holocaust of Pearl Harbor and the ensuing declarations of war both east and west set in motion a huge program of human blood donations for the benefit of the soldiers of this nation. Part of this blood was converted to plasma and part taken down to the albumin fraction. There resulted a large supply of left-over materials,

from which two substances pertinent to this review, thrombin and fibrin foam, were manufactured. The thrombin was of a considerably lower order of potency than that prepared by Seegers, with activity of 10 to 20 units per mg., yet this potency sufficed for clinical use.[19] The experimental and clinical experiences with this substance will be recited in the ensuing section on fibrin and other absorbable carriers of thrombin.

The parallel success of the thrombins prepared from three different species of animals was not unexpected to biochemists, since it had been shown by Quick[49] that thrombins obtained from various mammalian bloods appear to be identical, but they differ from bird thrombin and also from amphibian thrombin. Thrombin therefore appears to possess group rather than species specificity.

A word may be added as to the antigenicity of thrombin. Thrombin is protein in nature, and the unremoved impurities of the preparations likewise probably are proteins. It is possible theoretically to sensitize an animal of one species to the thrombin prepared from another, and this in fact has been successfully accomplished by Beatrice Seegal (personal communication) in guinea pigs and in rabbits. On the other hand, it can be stated that the use of a dissimilar thrombin (bovine) in clinical hemostasis has not brought indications of sensitization, and that there is considerable evidence to show that it will not do so. The case for this will be discussed in a forthcoming paper, together with the introduction of new data.[41]

One further aspect should be mentioned. The injection of thrombin into the blood stream is a dangerous procedure, apt to result in embolus formation, but the danger, to considerable degree, is a quantitative affair. One hundred units have been injected into a 285 gm. rat with no obvious disturbance,[63] and Seegal managed with care to instill 140 to 200 units into guinea pigs without evoking fatality from intravascular clotting. Transpose now the situation to clinical surgery, substitute a 70,000 gm. human being, and apply thrombin only to extravascular areas *toward which blood is flowing out of veins or arteries.* The likelihood of transport into the vascular system is remote, and the danger, should it occur, small. Here, too, positive experimental evidence exists to show that intravascular clotting does not occur, and that a venous channel remains patent beneath a rent repaired by a thrombin-soaked absorbable matrix, even though thrice performed. This experiment also will be related in a subsequent report.[42]

10. FIBRIN AND OTHER ABSORBABLE CARRIERS OF THROMBIN

The control of capillary ooze, and of bleeding from vessels scarcely larger than capillaries, has been one of the most vexing problems in the collection of insolubles that tumbled from that Pandora's box called neurosurgery. This type of hemorrhage, of so little consequence in most surgical localities, is both a supreme nuisance to the neurosurgeon and a risk to the life of his patient. Another type of hemorrhage of peculiar import is the flow from tiny but accessible arteries that lie upon structures too indispensable

to risk damaging by ligation, clip or cautery. Still a third type is the ominous gush from larger veins—the superior sagittal sinus in its posterior third, for example—the total occlusion of which means disaster to the patient. These examples have one thing in common: they bespeak the need for a substance with which to patch the bleeding area, just as one patches a tire, together with the means to vulcanize that material in place.

Cushing and his team of investigators in the Laboratory for Surgical Research began a hunt for such a substance 30-odd years ago. He teed off with the conjecture (1911) that:—"fibrin from whipped blood might be so prepared that it could be immediately plastered on bleeding surfaces, just as cotton is now used, and thus obviate the necessity for any subsequent replacement."[11] He was thinking evidently of improving on his practice of the day of saving well-solidified blood clots for implantation against bleeding points, but it is altogether probable that those clots retained traces of the uncombined primary factors of coagulation, especially thromboplastin and thrombin, which supplied an action quite apart from any influence of the fibrinous clot itself. However that may be, one of the assistant resident surgeons, Ernest Grey, was instructed "to find an absorbable material which might be used for this purpose," and succeeded, as reported (1915) in "Fibrin as a Haemostatic in Cerebral Surgery."[24] Grey used sheep's fibrin (as well as human blood) because it was readily procurable from the local Wassermann laboratory; washed it; soaked out the red cells; and sterilized it, apparently by autoclaving. Then he tested its effectiveness in halting bleeding, and found it to control hemorrhage better than wet cotton because "while fibrin probably exerts no appreciable chemical influence on the process of coagulation it appears to possess some mechanical property favorable to the formation of a firm clot." That mechanical property obviously is the rough texture which hastens agglutination of platelets and so starts the natural process of clotting upon its way. Grey recognized that "clotting may perhaps be hastened by dipping the piece of fibrin into a solution such as the Kocher-Fonio coagulen," but it was impossible to use that substance because it was not sterile and there was no way known of sterilizing it. It was used experimentally, however, for Harvey wrote:[25,26]

> The methods which have been used to combat these forms of hemorrhage [capillary ooze and venous bleeding] are of two types. Kephalin and the Kocher-Fonio coagulen are examples of the one type which depends upon chemical means to decrease the coagulation time of the blood. One objection holds true for all these substances. To apply solutions of this nature, some form of tampon is necessary, and in the removal of the latter, the clots are dragged from the hemorrhagic areas leading to secondary bleeding.

Thus did these surgeons of the first world war clearly visualize the problem, the solution of which was to rank high in the scientific achievements of the second. Harvey improved upon Grey's fibrin preparation by converting it to paper and plasticizing the protein with heat. If, to be sure, the fibrin of Grey and Harvey, unassisted by any active clotting agent, failed to survive in its intended role as a hemostatic (Cushing gave it a clinical trial),[25] its

sponsors had nonetheless performed a valued service by studying the reaction of tissues to the implanted material, and by comparing both the reaction and the absorption rate with similar factors connected with muscle implants. Fibrin was tolerated better by the body than muscle, and it disappeared earlier.

Fibrin then dropped temporarily from sight. Attention reverted to solutions and powders that coagulated blood upon their admixture. The later remarkable improvements in preparations of thrombin made that substance, by itself, a passably-good seal for bleeding areas. Still, the right combination of a patch and a vulcanizer did not appear.

a) *Fibrin Foam.* In 1944, Ingraham and Bailey[37] reported upon the successful use of a matrix of fibrin to carry a solution of thrombin to the site of hemorrhage, and to hold it there while clotting took place. The fibrin, prepared by E. A. Bering, Jr.,[4] was made as spongy and porous as possible so as to multiply the surface area upon which active clotting could occur. This sponginess proved valuable also in another direction. If the matrix was squeezed out before application (or sucked dry of its excess solution of thrombin through a cotton pledget immediately after implantation) it tended to take blood into itself by swelling, as is the habit of a sponge, thus insuring a thick substantial clot rather than a film at the surface. Adhesiveness was gained by the direct precipitation of fibrin, aided (probably) by the gluing effect of the blood platelets which sprouted to life at the moment of the clotting reaction.

Surgical operations in monkeys, and in 95 patients, 18 of whom subsequently yielded up the tissue upon which it was implanted, either by autopsy or at reoperation, served as the proving ground. The results were gratifying: the hemostatic action of the fibrin-thrombin combination was found to be speedy and reliable in control of ooze and venous bleeding, and histological studies showed that the fibrin pledgets were rapidly absorbed and excited a minimal tissue reaction. Subsequent studies[2,38,39] supplied anew the comparison of fibrin with muscle, and confirmed the conclusions reached by Harvey and Grey that, of the two, fibrin is tolerated better and absorbed more quickly. Additional comparisons were made with bone wax, with black silk sutures, and with oxidized cellulose. Meanwhile quick advantage was taken of the by-products accumulating from the program of blood fractionation in the production of serum albumin, and preparation of fibrin foam was begun in quantity for the armed forces. Woodhall[66] has reported recently upon its use in 226 operations in rehabilitation neurosurgery, and no one reading the details of his report can fail but share to some degree his optimism for the method.

b) *Oxidized Cellulose:* See Section 6.

c) *Starch Sponge.* A third absorbable material, prepared from starch,[5] deserves listing because with further improvements it may perhaps become a useful item. The specimens examined have been too friable and structureless for surgical handling.

d) *Gelatin Sponge.* In the writings of Bering, and of Ingraham and Bailey, great prominence was given to the fact that fibrin foam is derived from human and not from animal blood. Without entering upon the controversial questions implied in this stand, it can be pointed out that all parties interested in fibrin foam have been keenly aware of the fortuitousness of its existence, dependent as it has been upon the nation-wide program of human blood donations due to the war. Anticipating that either these donations, or the subsidiary program of conversion of blood to serum albumin, would one day cease to exist, two chemists, Correll and Wise, began well over a year ago the search for a substitute material. This they have found in gelatin.[9]

The choice of gelatin was inspired. Gelatin is a peculiar protein compound, rich in glycocoll, proline and arginine but poor or entirely deficient in the amino acids containing aromatic radicals upon which both the anaphylactic reaction and the precipitin reaction depend.[58,64] Gelatin, therefore, is nontoxic, it fails to produce anaphylaxis, and it has lost all trace of its species identification. It is a "universal protein."

The next step was to produce a matrix satisfactory to the surgeon and absorbable by the body. In this they succeeded fully. The resulting sponge weighs but 9 mg. per cc., absorbs 50 times its weight of water and, what is more important, takes up 45 times its weight of blood. It can be produced in pieces of any size and shape. It is tough, cuts easily without fragmenting, and resists rough handling. When wet, it plasters to the irregularities of the surface upon which it is laid. Digestion studies with a standard pepsin solution have shown that digestion occurs in about 30 minutes, a value similar to that for fibrin foam. Absorption studies in rats revealed that disappearance was complete in 30 days while nodules of fibrin foam persisted beyond 50 days.

The future of the thrombin-absorbable matrix method of hemostasis therefore seems assured, notwithstanding the recent cancellation of the program for manufacture of serum albumin. Moreover, certain improvements have been gained in the new gelatin sponge, notably as regards efficiency and surgical handling. The material has been submitted to study in a number of investigations, and a report on one of these, its use in neurosurgery, as studied both in monkeys and humans, appears elsewhere in this journal.[42]

CONCLUSION

The progress of neurosurgery has been paced by the successive advances in the technique of its most difficult phase, hemostasis. In neurosurgery the use of the ligature, so indispensable to surgery in general, is rendered impracticable due to the nature of the nervous system and to the conditions that govern the surgical approaches to its contents. In this paper, ten substitute methods for obtaining hemostasis have been listed and evaluated, not only for the attention of neurosurgeons, but equally as a guide to general

surgeons and those of the other specialties, since many of these hemostatic aids have wide fields of application. Some of the methods, such as bone wax, the Cushing clip, the electrocautery and hot water, are old standbys with well-established reputations. Some indeed are obsolete, as with the styptic and the several forms of thromboplastin. Some are new and experimental, and can be reviewed only by giving critical regard to the evidence upon which they have been recommended.

No one of these methods suffices to bring an operation to a successful conclusion. The surgeon is well advised to have most of them at hand and, to a very considerable extent, his surgical skill can be measured by the versatility, the correctness and the confidence with which he brings them into play.

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SURGICAL INVESTIGATION OF A NEW ABSORBABLE SPONGE DERIVED FROM GELATIN FOR USE IN HEMOSTASIS*

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IT IS the purpose of this paper to report upon the surgical and histological investigation of a new absorbable material derived from gelatin, for use as a thrombin carrier in hemostasis, which was introduced recently by Correll and Wise.[1] The literature covering absorbable substances, and a discussion of the position of these substances in the general field of hemostasis, was given in an earlier paper[2] and will not be repeated here.

DIRECTIONS FOR USING GELATIN SPONGE IN HEMOSTASIS

The physical qualities of gelatin sponge are surprisingly satisfactory for surgical use. The forms in which it can be supplied have no limit either of

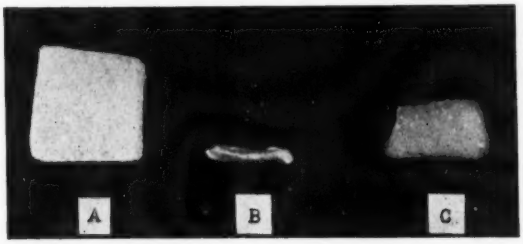

FIG. 1. Three pieces of gelatin sponge originally of equal size (15 mm. cube). (A) The dry material. (B) Reduction of volume when dampened with water and squeezed out. (C) Expansion after re-wetting (when fully immersed in water it resumes the shape of A).

size or of shape. The material is exceedingly light in weight, being less than 1 per cent of the weight of water. It is tough, resists rough handling, and cuts readily without tendency to fragment or disintegrate. Sheets of the dry material as thin as 2 or 3 mm. may be sliced by the surgeon with an ordinary scalpel.

* The animals were provided by the Upjohn Company, Kalamazoo, Michigan. The bovine thrombin[3] and the gelatin sponge constituted Upjohn research preparations. The fibrin foam and the human thrombin utilized in this study were prepared by the Upjohn Company in collaboration with Dr. Edwin J. Cohn of the Department of Physical Chemistry, and the Plasma Fractionation Laboratory, Harvard Medical School, Boston, Massachusetts, from blood collected by the American Red Cross, under a contract recommended by the Committee on Medical Research between the Office of Scientific Research and Development and Harvard University. The fibrin foam used came from jars sorted out from a regular production lot because of minor imperfections.

The sponge (see Fig. 1) is prepared for use in hemostasis by soaking in a solution of thrombin. Any concentration of thrombin may be employed, but our experience indicates that a good selection for neurosurgery is a solution containing 100 units (Upjohn)* per cc. Since the thrombin as packaged contains 1500 units per vial, the addition of 15 cc. physiological salt solution to the vial yields this result, and the amount is generally adequate for completing a major neurosurgical procedure; only occasionally does a second vial need to be opened.

The technique of wetting the dry gelatin sponge needs to be competently mastered by the surgical nurses. In its dry state, the sponge merely floats upon water; in a partially moistened condition the air retained in the cells prevents satisfactory shrinkage when squeezed out, or subsequent expansion upon contact with a liquid. Like any sponge, it must be *completely* wetted before being put to use. This is done by working it vigorously in the damp fingers to moisten the cell walls and expel air from the numerous pores; it will then engorge liquid readily and resume its shape under water. It may be squeezed out and re-used indefinitely. There is no need, of course, to wet the sponge in water however; wetting should be done directly in the thrombin solution which it is intended to carry.

It is convenient to have a few pieces immersed in the basin of thrombin at the beginning of the operation. When need for the material arises, one of two courses may be followed. The nurse may lift out a piece, blot off the excess thrombin upon a dry towel or gauze sponge, and lay it down convenient to the surgeon's use; the sponge shrinks; then, when laid upon a bleeding surface it engorges blood so that clotting occurs in the meshes. The second method is to lift the material, dripping, from the thrombin basin and apply it directly upon the bleeding area, depending upon suction applied through a cotton pledget to empty it of thrombin and allow secondary engorgement with blood. There is no practical difference between the two methods and the second is often the quicker in an emergency. Even in the first case it is helpful to lay down a cotton pledget on top of the sponge to press it into place, and touch this with the sucker. The pledget should be left unattended for 10 seconds or so while the underlying sponge swells with blood, and the blood clots. The cotton pledget is then loosened from the sponge by adding a drop or two of water, and is peeled away.

Special maneuvers are of value in favorable situations. If the bleeding point (a tear in the sagittal sinus, for example) can be held temporarily by a cotton pledget backed by suction. cut a piece of gelatin sponge of about the same size as the pledget and lay it alongside on the dura. Then cover this with a second pledget and slide the two pledgets across so as to bring the sponge above the tear in the vein. Often this can be done bloodlessly. In the event that bleeding is copious and the flow cannot be held back long enough to implant the matrix accurately, choose a piece larger than usual, and drop it, dripping wet with thrombin solution, into the pool of blood. Follow quickly with a cotton pledget and the sucker. The thrombin concentration of the order of 100 units per cc. affords a momentary delay before clotting sets in and it is possible often to seat the sponge matrix upon an unseen vessel, squeeze out the thrombin with the cotton pledget, and suck the cavity dry even though the procedure is done beneath a pool of blood. Obviously there is a good deal of chance in this, but it succeeds often enough to be tried.

There is one feature of the method that needs to be understood clearly. While a thrombin-carrying sponge may in truth be compared to a patch, it is a patch quite unlike the impervious patches of rubber, adhesive tape or cellophane common to household use. It becomes impervious only after blood has flowed into it and the clot sets up. *Blood therefore must flow well through the matrix* if it is to be fully utilized. If the outer surface of the sponge remains colorless after hemostasis is achieved, one of three errors has been made: bleeding was retarded too much by pressure; the solution of thrombin was too concentrated; or the piece of sponge was cut too thick. The selection of the two latter factors is simply a matter of personal experiment.

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* The Upjohn unit of clotting activity is defined as follows:[1] if 0.1 cc. of a thrombin solution clots 0.5 cc. of a specially oxalated bovine plasma in 15 seconds, that solution is considered to have a potency of 30 units per cc. This definition is followed throughout the paper unless otherwise indicated.

We prefer the gelatin sponge to be cut in sheets roughly 4 to 6 mm. thick when used with bovine thrombin 100 units per cc. Sometimes a heavy flow of blood calls for thicker sheets, but in general one should not employ sheets thicker, or larger in area, than will be reddened with blood throughout most of their extent. No harm results from the extra gelatin, but since secure hemostasis depends upon the clotting in the meshes, the filling of the meshes should be complete, aided if necessary by permitting extra bleeding to occur.

Once the sponge is seated over a vessel and clotting has occurred, it should be left undisturbed. Adhesion of the sponge to the tissues depends upon the precipitated fibrin aided probably by the gluing effect of blood platelets, and this adhesion, if loosened, is permanently spoiled. A new piece should be implanted if this does occur. On the other hand, well-attached patches of sponge are not easily brushed off and much work can be done in their vicinity. The commonest error is to pick them up with the sucker.

PREVIOUS INVESTIGATIONS

Correll and Wise[1] tested gelatin sponge after manufacture in rats and rabbits to be certain that it was non-antigenic, and found this to be true. They measured its digestion time, using a standardized technique which employed a solution of 1 per cent U.S.P. XII pepsin and found that 100 mg. pieces were digested in about 30 minutes, a value similar to that for fibrin foam. They undertook absorption studies in rats using gelatin sponge, starch sponge and fibrin foam, and they made a preliminary trial of gelatin sponge soaked in penicillin, 5000 Oxford units per cc. The penicillin made no difference to the absorption time; starch sponge was found to disappear in 10 days, gelatin sponge in 30 days, and nodules of fibrin foam were still visible at 50 days.

SURGICAL INVESTIGATION OF GELATIN SPONGE IN MONKEYS

Method. Sixty-seven operations were performed in 56 monkeys (*Macacus rhesus*) to determine the hemostatic effectiveness of gelatin sponge, the reaction of the tissues to the material, its rate of absorption, and the comparison of these factors with fibrin foam implanted at the same procedures. Pieces of both materials (gelatin sponge and fibrin foam) were cut to the indicated sizes in the dry state. They were soaked in thrombin, and blotted to dampness on gauze before implanting.

Five sites of implantation were chosen, all in the cranial chamber. They are serialized as follows:

Series A. Epidural, on the incised and bleeding superior sagittal sinus.
Series B. Subdural, on intact brain. No intended bleeding.
Series C. Subdural, on pricked and scarified brain.
Series D. A block of cortex removed and replaced by the matrix.
Series E. Subcortical implant.

Sterile surgical technique was followed. General anesthesia (cylopal, 100 mg. per kg. of body weight) was given intraperitoneally about 30 minutes before operation. The scalp was shaved and prepared with soap and water, ether and mercresin. A sagittal incision was made, permitting craniectomy across the midline in the case of Series A, or bilateral unjoined parietal craniectomies in the other groups.

In *Series A* the superior sagittal sinus was opened by an incision 5 mm. long. Bleeding was held in check with a cotton pledget while a piece of gelatin sponge was laid alongside, covered with a second cotton pledget, and slid across to seal the opening. It was found necessary to permit some bleeding to take place into the sponge by removal of pressure to fill the sponge well, since the concentration of thrombin chosen for the experiment (300 units) was probably stronger than the optimum for hemostasis. Fibrin foam was then similarly applied to the sinus at a point farther back.

In the other series, with bilateral craniectomies, the dura was opened on each side. In *Series B* the matrix was slipped beneath the dura to lie on intact brain. In *Series C* the surface of the brain was first punctured by multiple needle pricks and scarified with the scalpel to promote bleeding, and the hemorrhage was then controlled by the hemostatic matrix. In *Series D* a block of cortex was resected from the top of a gyrus and the material was laid in its place. In *Series E* a stab wound was made in the cortex, a pair of dissecting scissors inserted to a depth of about 2 cm., the points spread, and a piece of material inserted into this tract.

The dura was closed with 1 or 2 sutures, and the scalp edges were brought together with a row of buried interrupted sutures and a continuous buried subcuticular stitch. Silk was used throughout. Only one postoperative infection developed, and this subsided with the administration of topical and intramuscular penicillin. This animal is included in the Series (Experiment IV), but a duplicate animal was added.

Sacrifice was accomplished with an overdose of cyclopal (2 gm.). The head was removed on the bandsaw with a basal cut preserving the cerebrum and, after loosening the scalp up to the craniectomy edge, was immersed in 10 per cent formalin. Later, the scalp was removed and blocks representing the site of implantation were cut out. After further fixation in formalin, sections were cut, stained with hematoxylin and eosin, and mounted.

EXPERIMENT I. 36 animals

Matrix: Both gelatin sponge and fibrin foam; pledgets cut 4×6×10 mm.

Thrombin: Bovine thrombin 300 units per cc.

Sacrifice calendar: 3 days, 6 days, 12 days, 20 days, 30 days, 45 days, 60 days, and (for Series E) 120 days.

Histological Studies (See plates I to V).

Series A. At 3 days, both fibrin foam and gelatin sponge were well adherent to dura and filled with blood cells and fibrin. There was no peripheral reaction. By the 6th day, giant cells began to appear and, by the 12th, lymphocytic reaction occurred. The giant cells tended to invade the material and apply themselves to its fibers. At the 20th day, the material was broken up and lymphocytes and giant cells were still present. At the 30th day, only occasional broken fibers were seen and there was slight lymphocytic reaction. At 45 and 60 days, no material was found and there was no recognizable reaction. No evidence of intravascular thrombus formation at any stage.

Series B. The gelatin sponge was uniformly attached to dura and not adherent to brain. At 3 days, both materials showed red cells and fibrin in their meshes, with a few leucocytes. Through the 12th day, there was no reaction beyond a moderate increase in leucocytes in parts of the borders of the implants. At the 20th day, broken strands of each material remained and there was lymphocytic and giant cell reaction. At 30 days, only a few giant cells remained, in some of which ingested fiber remnants were seen. At 45 days, only an occasional nest of giant cells remained at the site of the implant and at 60 days, there was no trace of reaction on dura or brain surface.

Series C. Again the sponge attached itself to dura rather than brain. At 3 days, both substances contained blood and fibrin in their meshes. The gelatin sponge meshes were filled more completely than those of the fibrin foam. At 6 days, there was minimal leucocytic reaction within the material, which lay loosely on the brain surface. By the 12th day, the lymphocytic and giant cell reaction was marked. The brain tissue itself took no part in the reac-

tion. Its surface was smooth and the material was loosened from it. Both materials were still present at the 30th day, with some lymphocytic reaction and giant cells engulfing fibers. At the 45th day and 60th day, there was no remaining evidence of the implant.

Series D. At 3 days, both substances contained blood and fibrin and were well attached by clot to the adjacent brain. Only a few leucocytes were present. By the 6th day, phagocytes were appearing and there were fibroblasts developing in the clot. The material was becoming loosened from the brain and tended to come off with the dura. At the 12th day, lymphocytes, with some leucocytes and phagocytes and a few giant cells, were surrounding and invading the material. At the 20th day and 30th day, the reaction was about the same, with conspicuous invasion of the material by the reactive cells, while the peripheral brain tissue showed minimal reaction.

At the 45th day, a pseudo-cystic space representing the area of the sponge implant remained roofed by meninges, having in its floor only a few giant cells with engulfed gelatin sponge, and a few lymphocytes and phagocytes. In the case of the fibrin foam, a small, collapsed, bloodless remnant remained, with no appreciable reaction.

At 60 days, a few giant cells were found among the loose fibers of the meninges between the brain and dura and the brain surface was without reaction.

Series E. Through the 12th day, the reactions to both substances were comparable to those of Series D. At the 20th day, both substances had nearly disappeared. A little fibrin foam was present in the 30th day specimen, while the gelatin sponge was seen only as a few fibers engulfed in giant cells. By the 45th day, there remained only a few phagocytes and the glial reaction which would be expected in the injured area.

EXPERIMENT II. 4 animals

Matrix: Both gelatin sponge and fibrin foam; pledgets cut 4 × 6 × 10 mm.
Thrombin: Bovine thrombin 300 units per cc.
Calendar: Two operations were performed in each animal, identical implantations being made on each occasion. The number of days elapsing between the 1st and 2nd operations was 119, 139, 132 and 128 days respectively for Series A, B, C, and D. All animals were sacrificed 30 days after the 2nd operation.
Implantation sites: A, B, C and D.

Surgical Note on Conditions Found at 2nd Operation. No matrix remained in any location. *Series A:* Only slight scar was encountered during the approach to the sagittal sinus, and the sinus was uncovered without difficulty. Sinus re-incised. Bleeding free. No evidence of thrombus. *Series B:* Fine adhesions between dura and brain. *Series C:* Fine adhesions. *Series D:* Adhesions denser, but not greater than ordinarily seen following cortical extirpation.

Histological Studies (Series A, B, C, and D). There was no appreciable difference in reaction either to gelatin sponge or to fibrin foam when compared to similar tissues observed after a single implant. The progress of absorption of the materials was likewise similar.

EXPERIMENT III. 10 animals

Matrix: Both gelatin sponge and fibrin foam; pledgets cut 4 × 6 × 10 mm.
Thrombin: Human thrombin, 300 units per cc.
Sacrifice calendar: 3 days, 6 days, 12 days, 20 days and 30 days.
Implantation sites: A and E.

Histological studies showed no appreciable difference in reaction, with respect either to gelatin sponge or fibrin foam, in these animals in which human thrombin was used, when compared to that seen in the experiment in which bovine thrombin was used. The progress of absorption of the matrices likewise was indistinguishable.

EXPERIMENT IV. 6 animals

Matrix: Gelatin sponge; pledgets cut 5×10×10 mm.
Thrombin: Bovine thrombin, 1500 units per cc.
Surgical calendar: Operations performed at intervals of 3 days.
Sacrifice calendar: See Table I.
Implantation site: Series A only.

TABLE I

Calendar in days for 6 monkeys undergoing multiple operations to open and repair the superior sagittal sinus with gelatin sponge soaked in bovine thrombin, 1500 units per cc.

Monkey No.	Surgical Implants			Sacrifice (days after last operation)
	First	Second	Third	
55	0	3	6	Died 4 hr. p.o. without reacting from anesthesia
56	0	3	*	18
57	0	3	**	18
58	0	3	6	27
54	0	3	6	35
53	0	3	6	48

* Omitted due to poor general condition of animal.
** Omitted due to wound infection following second operation.

Surgical Note. It will be observed that 16 operations were performed in 6 animals, 10 of the operations being re-exposures of implants made 3 days earlier. This program afforded an opportunity to observe certain significant facts about vein repair as done by the thrombin-matrix method.

On 10 occasions the previously implanted sponge was peeled away in order to substitute a new piece. Three times spontaneous fresh bleeding occurred from the sinus as this was done, while on 7 occasions it was necessary to incise the soft gelatinous plug holding the vein edges together. In all 10 instances the sinus was found to be patent; bleeding was vigorous in 9, and sluggish in 1.

Of the 16 implantations of sponge soaked with thrombin, 15 held firmly. One, early in the series, came loose during closure, flooding the wound with blood and necessitating reopening and a new application. It was partly from this experience that we concluded that the concentration of the thrombin solution may in fact be too strong for secure hemostasis with the matrix method, since clotting then occurs at the surface without allowing thorough penetration of the sponge. However, by gently pressing the sponge up and down on the sinus it was found possible to work fresh blood throughout the meshes and thus continue the experiment unaltered.*

Histological Studies. M-55. This animal died 3 hours after the 3rd operation. The implanted material was visible grossly as a loose soft-textured mass. Microscopically, fragments of gelatin sponge were seen, loosely attached to dura, with no cellular reaction and with some blood in the meshes. *M-56.* A remnant of gelatin sponge was found imbedded in the dura, with

* This experiment was designed primarily to test for antigenicity to bovine thrombin, hence the high concentration. Data will appear in a forthcoming paper.[3]

practically no cellular reaction. *M-57* (wound infection). There was a considerable area of inflammatory reaction in the dura with leucocytes and lymphocytes. A few giant cells were found at a distance from the infected area which may represent the area of implantation. *M-58*. The dura showed only a few giant cells in the area of the implants. *M-54*. The dura was without evidence of reaction. *M-53*. Grossly the dura seemed somewhat thickened in the area of the implants, but there was no cellular reaction and no trace of material.

SUMMARY OF HISTOLOGICAL STUDIES

1. There is no appreciable difference in the reactions to fibrin foam and gelatin sponge when these substances are implanted under comparable conditions on dura, brain which is uninjured, injured brain, or beneath the cortex.

2. Up to 3 days, each absorbs blood and becomes surrounded by and filled with clot, and provokes no tissue reaction.

3. Tissue reaction in each case and in all positions studied begins about the 6th day, at which time leucocytes appear.

4. The maximum reaction in each case and in all these positions occurs by the 12th day, when lymphocytes and giant cells predominate. The giant cell response is a little more marked and a little earlier in the case of the fibrin foam.

5. Between the 20th and the 45th day the material tends to disappear, and the mechanism appears to include engulfment by giant cells. Disappearance is a little earlier in the subcortical implant than elsewhere.

6. After the 30th day, the reaction on dura and uninjured brain surface is negligible.

7. On severely injured brain, phagocytes and giant cells remain in appreciable numbers up to 45 days. The ultimate glial reaction is no more than would be expected from the injury alone.

8. Implants repeated in each position after an interval of 119 to 139 days show, after 30 days, no appreciable difference in reaction from that observed after single implants.

9. The use of human thrombin with implants of fibrin foam and gelatin sponge on dura seems to produce a reaction in all respects similar to that seen when bovine thrombin is used.

10. When implanted between dura and brain, gelatin sponge has a tendency to become glued to the dura while fibrin foam more often attaches itself to the brain.

CLINICAL EXPERIENCES

The possibilities for the use of the thrombin-matrix hemostatic aid are legion, and new sites and purposes are suggested frequently. The following notes represent a review of its use in 24 routine neurosurgical operations. Bovine thrombin was used throughout; 300 units per cc. in the first 4 cases done, 50 units in the next 3, and 100 units in the remainder. In two cases

death occurred, 3 days and 8 days following surgical operation, and the tissues were recovered at autopsy. The histological appearances of these corresponded closely to the similar stages in monkeys.

Cranioplastic Flaps (6). Two uses of the sponge stand out above all others here: the repair of torn venous sinuses and the control of dural ooze, especially that from hidden areas beneath the cranium. Analysis of the operative notes shows that rents in the superior sagittal or the transverse sinuses were repaired in 3 cases, ooze from the dura halted in all 6, the copious bleeding of pacchionian bodies in 2, and bleeding from a small cortical artery in the motor area in 1.

Subtemporal Craniectomies (3). These cases need to be considered singly. The first was a newborn baby of 2 days, with a subdural hematoma complete with membrane. A subtemporal burr hole, which proved inadequate for evacuating the clot, was enlarged with rongeurs. The dura was opened in stellate fashion and the hematoma expelled. The brain bulged and rapidly herniated through the opening, causing hemorrhage from the cortex. Partly to control this hemorrhage and partly to provide a temporary covering in lieu of dura, two sheets of gelatin sponge, thrombin-soaked, were laid across the opening and the wound was closed. In the second case, gelatin sponge was used between dura and bone, but for the control of arterial rather than of venous bleeding, several branches of the meningeal being readily halted when capped with thrombin-soaked sponge. In the third case the main trunk of the middle meningeal artery proved troublesome and successive bites with the rongeur failed to uncover it sufficiently to permit successful cauterization or clipping. Thrombin-soaked sponge was therefore pushed under the bone directly against the open-ended vessel with immediate success.

Suboccipital Craniectomy (1). An extensive exposure, including removal of the back of the foramen magnum and the arches of the atlas and the axis, met with an accident in the lateral recess between the base of the occiput and the atlas. Sharp bleeding occurred from a vessel which proved inaccessible to clip or cautery; the latter in fact caused contraction of occipital muscles at a distance, indicating proximity of the forceps to the 1st cervical nerve. The hemorrhage was held for a time with cotton packing, but bled afresh when this was removed. A piece of sponge measuring about $5 \times 5 \times 10$ mm., soaked in thrombin 300 units per cc., was applied and held in place with a cotton pledget, which was taken off in 30 to 45 seconds. Clotting had occurred on the under side of the sponge, although the top surface was still dry and swelled up with water which came upon it. The patch did not wash away during irrigation.

Elevation and Debridement of Depressed Skull Fracture (1). The thrombin-soaked sponge did real service here. A bashed-in forehead exposed dura, sagittal sinus and brain. The sinus was torn in 3 visible places and at least once beneath the intact portion of the cranium posterior to the fracture.

Bleeding was copious. The tears in the sinus, including the hidden tear, were quickly and securely "patched" with gelatin sponge.

Scalenotomy (2). While it cannot be said that any real need existed for the hemostatic sponge in these cases, some experience was gained and the opportunity was afforded in one case to compare the hemostatic action of oxidized cellulose* with that of thrombin-soaked sponge (100 units per cc.). Following section of the scalene muscle, minor bleeding occurred at the cut ends. A strip of oxidized cotton (without thrombin) was applied across the muscle stump. The cotton blackened as the blood reached it, but hemorrhage continued to flow around its edges; there was no tendency of the material to adhere, and its slight stiffness prevented it from forming to the contour of the surface on which it was laid. When pressure was removed, it came away of itself, and so was taken out. A piece of gelatin sponge 12 mm. square, soaked in thrombin, was then applied to the muscle end and bleeding stopped promptly. The material adhered and was left in place. A somewhat more important aid was rendered in this case by gelatin sponge in the control of small vessel hemorrhage alongside one of the cords of the brachial plexus. It is of interest too that the patient did not complain of radiating pain in the distribution of the plexus during the recovery period.

In the other case a small but persistent vein, lying adjacent to the internal jugular, was ineffectively controlled by cautery but stopped upon application of a 12×12 mm. stamp of sponge.

Carotid Arteriography (1). A small piece of gelatin sponge was used to stop the leakage from the hole left after extraction of the 18 gauge needle through which diodrast was injected into the common carotid artery.

Chondrectomy for Herniated Disk (10). The network of veins lying between the dural and bony spinal canals constituted the principal application of thrombin-soaked sponge in disk cases. Its success ranged from excellent when applied squarely upon the rent in a vein to failure when the hemorrhage came from unseen vessels overlain by dura, fat or nerve root. Visibility of the point of bleeding, while distinctly helpful, was not altogether essential, for if a large piece dripping with thrombin was pushed through the pool of blood and seated luckily, it usually held. On the other hand, a half dozen trials might fail, leaving one to the use of hot water and temporary pressure. Other uses should be mentioned. An unusual degree of hemorrhage from the intervertebral disk space, following curetting of fragments of a nucleus, prompted us to pack the space with 3 or 4 pieces of sponge. This succeeded in halting bleeding but it recalls another case in which oxidized cellulose (cotton) was used for the same purpose and with better effect. The relative stiffness and incompressibility of the cellulose appears to render it a better pack where pressure is required than the extremely compressible sponge. In another case the dural sheath of a nerve root was nicked, flooding the field

* Supplied by Dr. Virginia Kneeland Frantz.

with spinal fluid. This was quickly and permanently checked by patching the hole with thrombin-soaked sponge, made to adhere by first smearing it with blood. Another excellent service was performed by the material in controlling a vessel lying upon a nerve root at the 6th cervical level, avoiding completely any possible damage to the root by the heat from electrocoagulation.

These experiences suggest the following list of uses for thrombin-soaked sponge:

1. Control of capillary ooze.
2. Repair of veins.
3. Control of bleeding from small arteries, especially those lying upon structures likely to be injured by the clip or the cautery; or from larger arteries when backed by pressure of adjacent structures (i.e., the middle meningeal under the cranial ledge).
4. To seal a spinal-fluid leak. Added blood or plasma is necessary to form the clot in the matrix. It is probable that after closure of the dura with interrupted sutures the line of attachment can be made waterproof by this method.
5. To bridge a defect in the dura, either by use of the gelatin sponge alone, or of the thrombin-soaked sponge to which blood or plasma is added to form a smooth, impervious artificial clot in the framework of the sponge meshes. The histological studies are of considerable interest in this connection, since they show a consistent tendency for sponge to adhere to dura and not to brain.

CONCLUSIONS

1. Studies are presented of a new material, gelatin sponge, used as a carrier of thrombin for surgical hemostasis.
2. Surgical implantations (intracranial) in 56 monkeys, followed by histological studies, show that gelatin sponge is tolerated well by dura and brain, produces a slight cellular reaction not much greater than that formed in response to simple blood clots, and disappears by tissue digestion and phagocytosis in from 20 to 45 days, paralleling in these respects similar implantations of fibrin foam.
3. The use of gelatin sponge to repair torn veins (i.e., the superior sagittal sinus) is not attended by intravascular thrombus formation. The same veins were opened and repaired on 2 and 3 occasions, and their channels remained patent.
4. Experiences with gelatin sponge as a hemostatic aid are reported in connection with 24 routine neurosurgical operations.
5. Directions are given for using gelatin sponge as a hemostatic agent.

The authors wish to express their appreciation to Mr. Stuart L. Long for his excellent care of the animals; to Miss Betty Johnson, R.N., who acted as surgical assistant; and to Miss Hilda Mae Cairns, who made the histological preparations.

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PLATES

The five plates of photomicrographs illustrate the five series of implantations of gelatin sponge made in *Macacus rhesus* monkeys. The tissue reactions at different stages and the progress of absorption of the gelatin sponge are thus recorded for 3-day, 6-day, 12-day and 30-day intervals after surgical implantation.

The magnification used throughout is 280 diameters. The photomicrographs have been placed with the tissue at the left and the gelatin sponge implant at the right.

PLATE I

Series A. Gelatin Sponge Implanted Epidurally, on the Incised and Bleeding Superior Sagittal Sinus.

FIG. 2.—3 days. Gelatin sponge attached to dura by clot. Meshes filled with red cells and fibrin. No cellular reaction in dura.

FIG. 3.—6 days. Material well preserved. Clot in meshes. Early cellular reaction in dura.

FIG. 4.—12 days. Material breaking up. Marked lymphocytic and giant cell reaction.

FIG. 5.—30 days. Material broken and disappearing. A few giant cells remain.

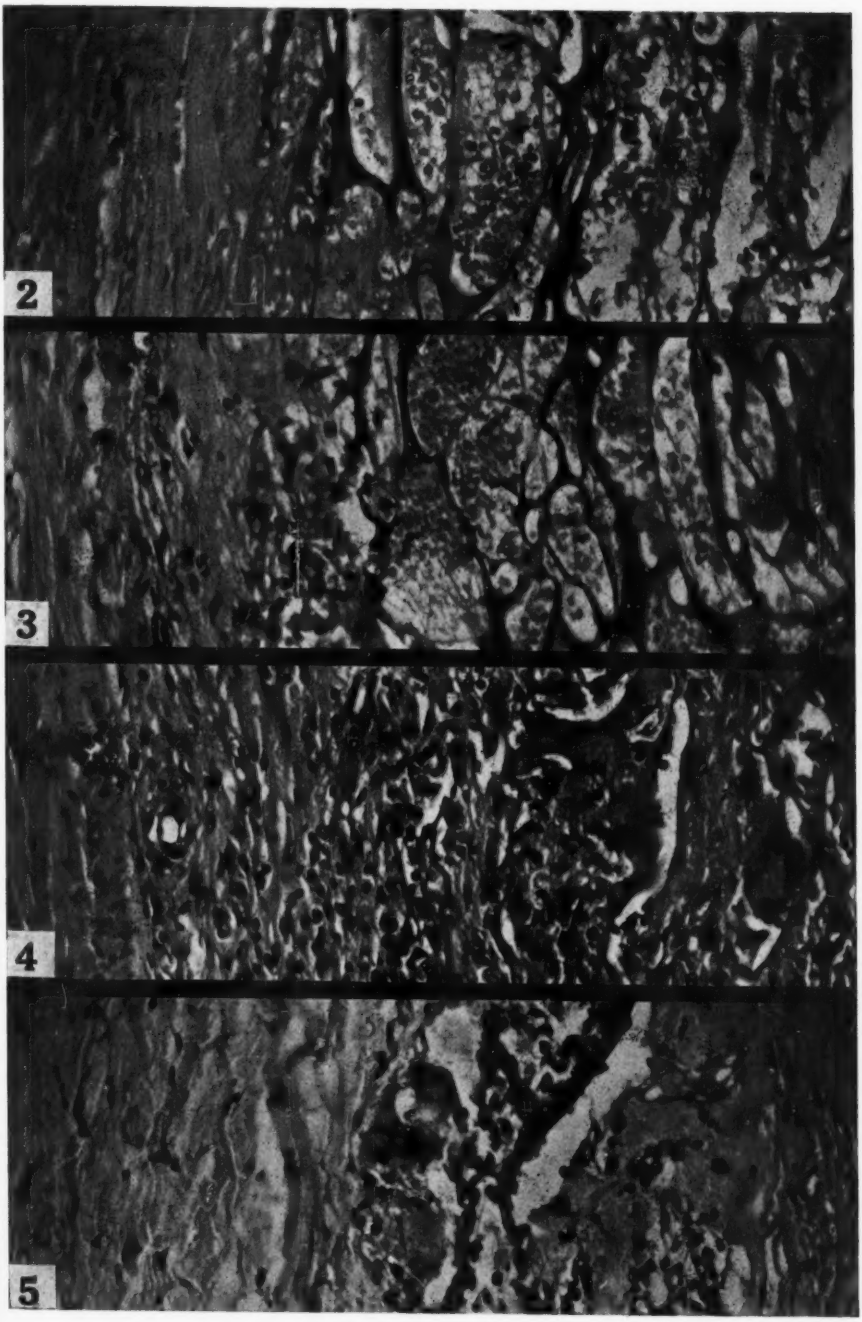

PLATE I

PLATE II

Series B. Gelatin Sponge Implanted Subdurally, upon Intact Brain. No Bleeding Intended.

FIG. 6.—3 days. Gelatin sponge separated from brain. Small amount of blood in meshes. No cellular reaction.

FIG. 7.—6 days. Material closely applied to the brain surface. Note the absence of cellular reaction in brain.

FIG. 8.—12 days. Material separating from brain and breaking up. Giant cells and a few lymphocytes among fibers. No reaction in brain.

FIG. 9.—30 days. No visible material. A few nests of giant cells in the leptomeninges. Some of these, not seen in the photograph, contained fragments of material.

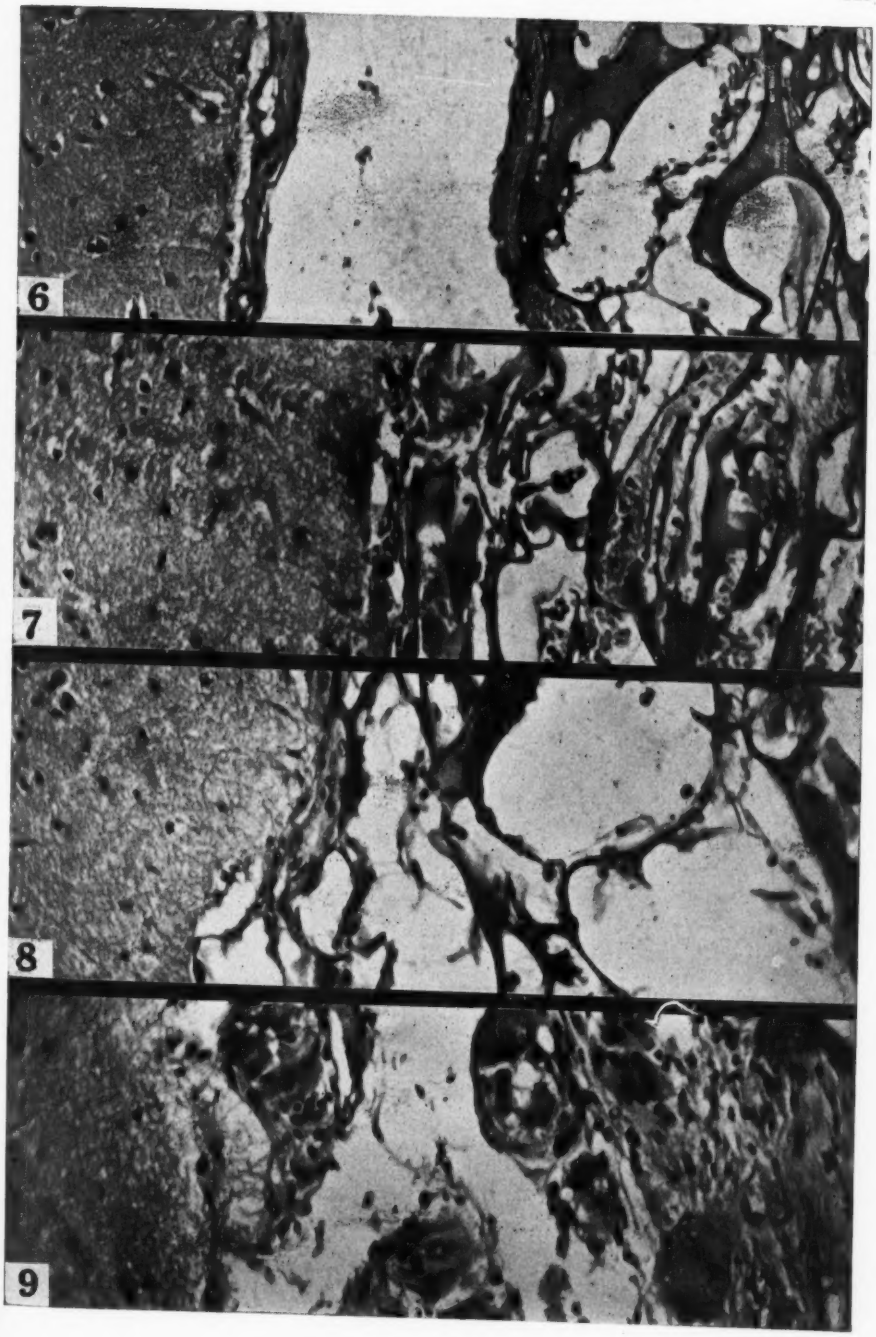

PLATE II

PLATE III

Series C. Gelatin Sponge Implanted Subdurally, on Brain Surface which Has Been Pricked and Scarified to Produce Bleeding.

FIG. 10.—3 days. Gelatin sponge. In this preparation the material has become separated from brain and the photograph shows only the clot in the meshes.

FIG. 11.—6 days. Material has separated from brain and is beginning to swell and break up. The clot still remains in the meshes. No reaction in brain.

FIG. 12.—12 days. The material in this section is adherent to dura. Note that there is no tendency to stick to brain. The cellular reaction is minimal but where it does occur it originates from the meninges.

FIG. 13.—30 days. The material is breaking up. Giant cells lie in the meshes. A few lymphocytes in the meninges. No reaction in brain.

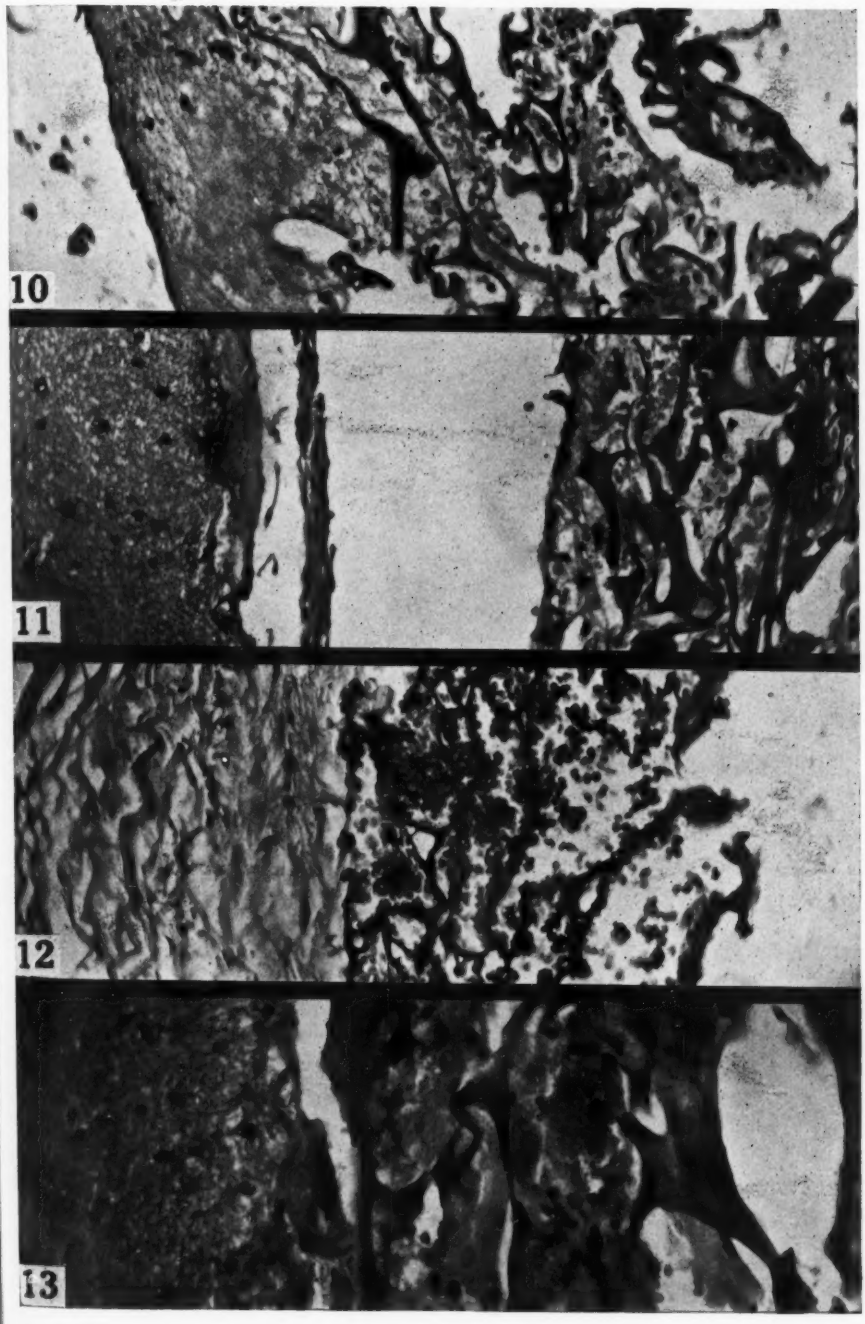

PLATE III

PLATE IV

Series D. Gelatin Sponge Inserted into the Recess from which a Block of Cortex Has Been Removed.

FIG. 14.—3 days. Gelatin sponge with erythrocytes, fibrin and a few leucocytes in meshes. At the left of the picture lies injured brain with hemorrhage at the edge toward the sponge.

FIG. 15.—6 days. This picture is similar to that at 3 days. There is minimal phagocytic reaction at the border of the material.

FIG. 16.—12 days. The fibers of the sponge are thinned out and disappearing. There is still blood in the meshes. Phagocytic reaction has increased and a few giant cells have appeared.

FIG. 17.—30 days. Fibers of sponge are still visible, but the meshes contain only lymphocytes and giant cells. The adjacent brain shows no cellular reaction.

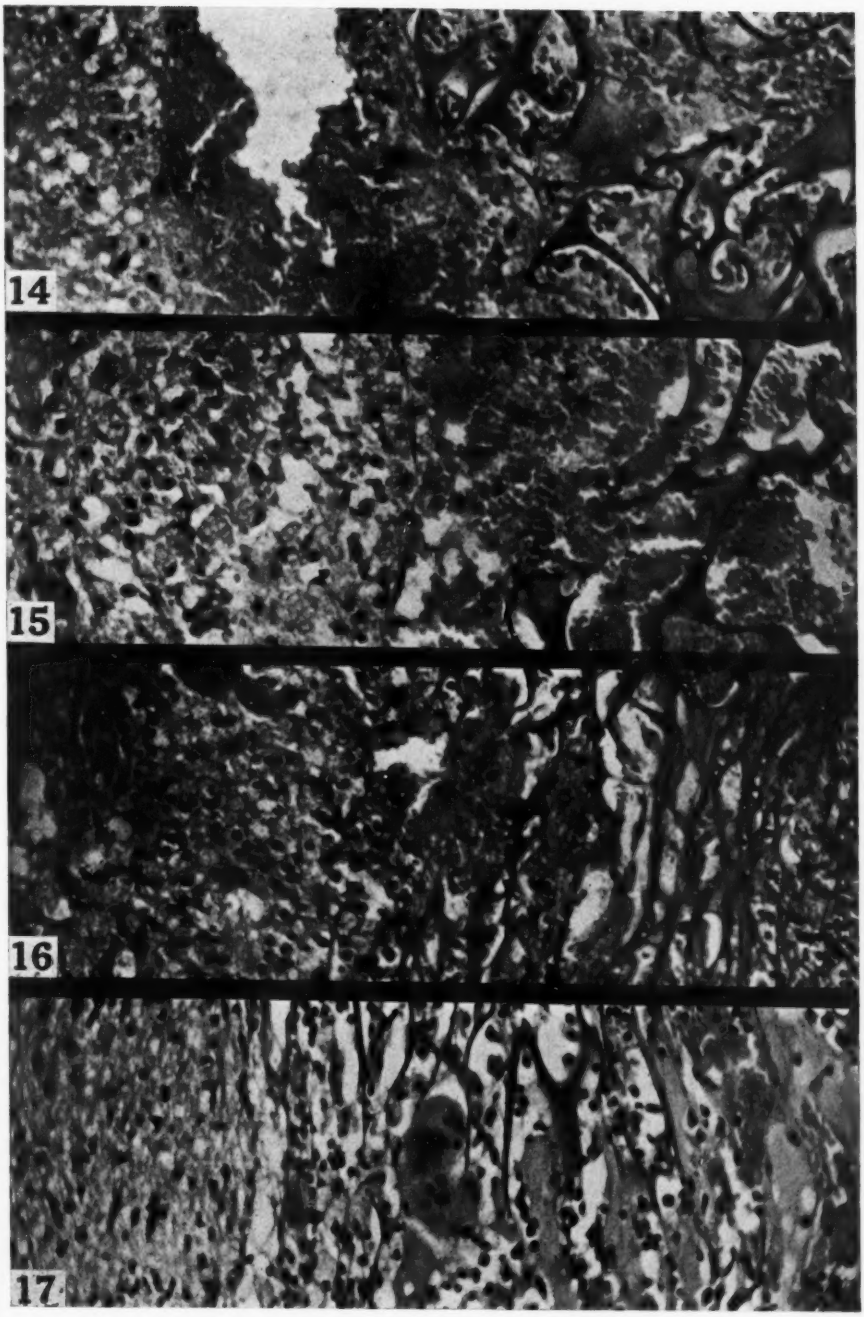

PLATE IV

PLATE V

Series E. Gelatin Sponge Inserted Subcortically in Brain.

FIG. 18.—3 days. Gelatin sponge imbedded in brain, showing erythrocytes and fluid in meshes. No reaction in brain.

FIG. 19.—6 days. There is a minimal phagocytic reaction at border of imbedded sponge.

FIG. 20.—12 days. The sponge has disappeared, leaving only a few giant cells and an island of phagocytes.

FIG. 21.—30 days. The site of the implantation shows phagocytes, a few giant cells and slight glial proliferation.

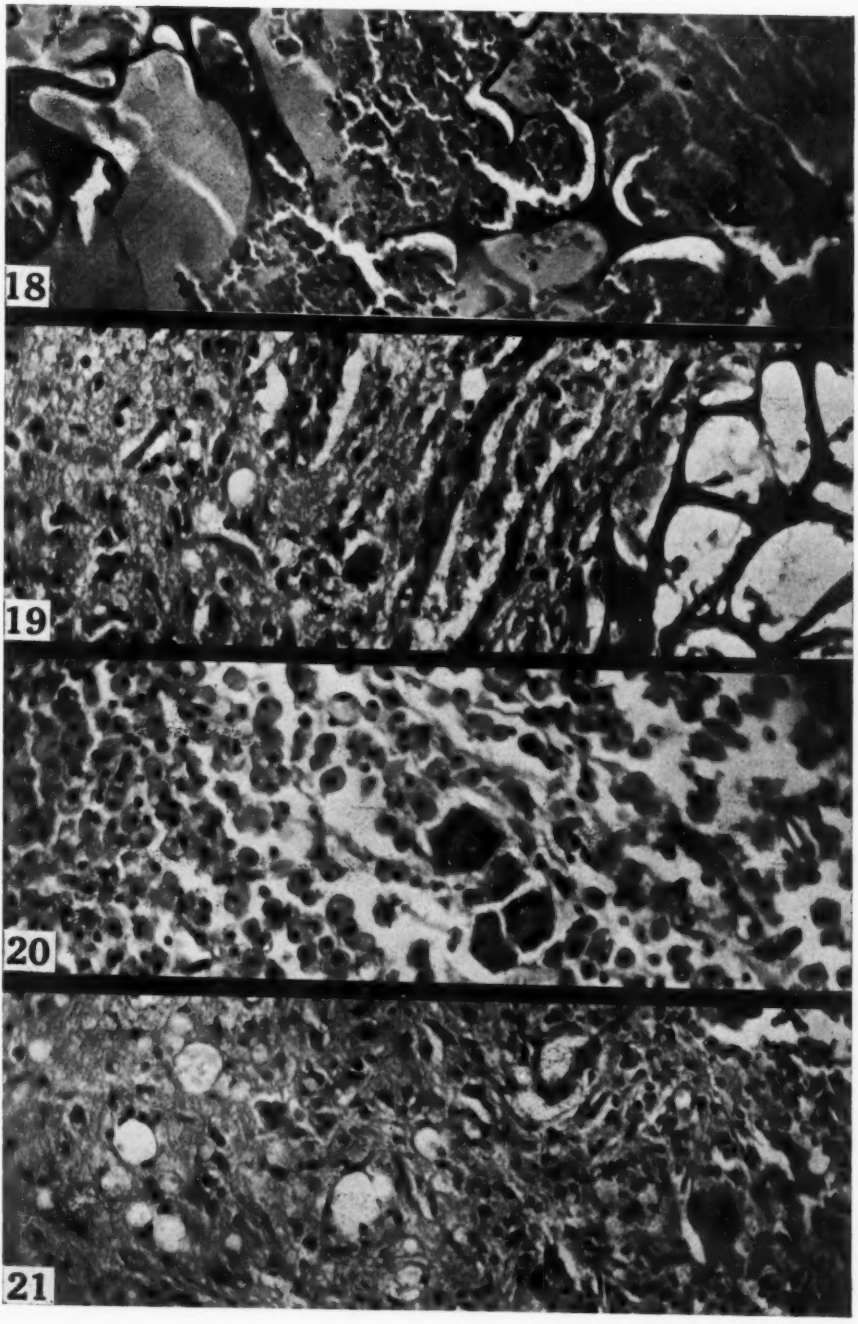

PLATE V

CLINICAL NOTES AND NEW INSTRUMENTS

BRAIN ABSCESS METASTATIC FROM THE LUNG. RECOVERY FOLLOWING PENICILLIN THERAPY AND REPEATED ASPIRATION

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Recovery from metastatic brain abscesses, particularly those secondary to pleuro-pulmonary suppuration, is infrequent. Only three cases[3,8] can be added to those compiled by King[4] in 1936. Since the result of treatment of other types of brain abscess is much better, the reason for the almost universal inadequacy of present-day therapy must be sought in the inherent character of the metastatic brain abscess. In many cases there are multiple foci, but the consensus of the various estimates[1,6,7] is that probably more than 50 per cent of such abscesses are solitary. This would leave more than half of the cases amenable to surgical therapy.

Since Grant[2] directed our attention to the relation of the mortality in brain abscess to the timing of the operation, better results have been obtained by delaying operation until the abscess has encapsulated. With abscesses metastatic from the lung, and particularly with putrid pulmonary suppuration, the experience of many observers has been that the brain abscess does not show the tendency to localize and encapsulate as promptly and as completely as does the brain abscess secondary to nearby suppurative foci. Charrier and Ferradou[1] state that a capsule is never found with anaerobic bacteria.

Up to the case about to be reported we had not had any recovery from a metastatic abscess of the brain secondary to lung suppuration in eighteen cases. In several instances of well encapsulated single abscesses, we believe some technical error contributed to the fatal issue. In the other cases, however, there was no evidence of encapsulation. It was lack of the tendency to encapsulate that led King[4] to propose and successfully carry out early and radical removal of the uncapsulated involved brain. With the advent of penicillin it was hoped that its administration would so modify the pathogenesis of the metastatic brain abscess that subsequent surgery might be successful.

CASE REPORT

(J. H. #527568) A 48-year-old married man was well until August 1944, when he developed cough and malaise and thought he had a "cold in his chest." After one week of this "cold" he suddenly developed sharp severe pain in the left lower chest, for which his chest was strapped and a diagnosis of pleurisy made. When he developed persistent fever, he was treated with sulfonamide with the diagnosis of left lower lobe pneumonia, but he failed to improve and was consequently transferred to a hospital near his home. There a diagnosis of empyema was made. This was treated by means of thoracic aspiration for two weeks until a diagnosis of lung abscess was made. The ninth rib was then resected and the patient treated by open drainage of the abscess cavity and intramuscular penicillin. Although the patient's sputum was never foul, the left lower lobe lung abscess which was found at thoracotomy (5 weeks prior to admission to Mount Sinai Hospital) was reported as containing foul pus.

The patient was discharged one week after operation and the sinus tract was allowed to close gradually. Eleven days prior to admission, the patient again developed malaise, cough and fever which rose to 103°. His local physician found the wound discharging thick, greenish, foul pus and inserted a catheter drain. At this time the patient complained of a right-sided headache.

Suddenly, two days before admission, this mentally normal patient began to answer questions and express himself with unintelligible words and jargon. He could neither name objects nor carry out acts intelligently. In this condition he was brought to this hospital.

Examinations. The chest was somewhat emphysematous and below the left scapula dullness to percussion and distant breath sounds were noted. The thoracotomy sinus was draining foul greenish pus. The patient had no cough.

Neurologically, the patient was aphasic in all spheres. He was unable to name objects which he saw and felt. He was unable to read, and when given a newspaper held it upside down. He was unable to use simple objects intelligently and was unable to follow simple directions.

The left temporal region of his skull was exquisitely tender. There was slight weakness of the entire right side with an attendant hyperreflexia; there was slight right hemihypalgesia.

FIG. 1. Antero-posterior view of the abscess cavity after the injection of lipiodol.

The left pupil was larger than the right and he showed bilateral Babinski response. At times a right homonymous hemianopia appeared to be present but it was difficult to evaluate any of the patient's responses.

A lumbar puncture at this time showed a crystal-clear fluid with an initial pressure of 110 mm. The fluid contained 510 cells, mostly lymphocytes, 4 plus Pandy with 180 mg. of protein. The electroencephalogram indicated an active left temporal focus.

Treatment. The patient was given intramuscular penicillin, 20,000 units every three hours day and night.

Nine days later he became drowsy and unresponsive; the pulse slowed to 64. A trephine opening was made near the left coronal suture and a brain cannula inserted. Three cm. below the dura there was very slight resistance and the brain abscess cavity was entered from which was aspirated 20 cc. of non-foul greenish pus. 50,000 units of penicillin were injected into the abscess cavity in 5 cc. of saline and the patient was returned to the ward with the trephine wound packed open. The pulse shortly thereafter rose from 64 to 84.

A smear of the pus showed no organisms, but Streptococcus hemolyticus B was reported in one culture as well as Gram-positive chain-forming cocci which failed to grow out.

The first operation was on November 29, 1944. Three days later the patient again became drowsy and the pulse slowed to 62. A brain cannula was introduced and 25 cc. of somewhat thicker pus was removed by aspiration and 50,000 units of penicillin along with ½ cc. of lipiodol were instilled into the abscess (Figs. 1 and 2). At that same time the chest condition was so greatly improved that the drainage sinus was allowed to close.

By December 13 the patient had received 3,380,000 units of penicillin intramuscularly over a period of 23 days, and this therapy was discontinued.

Altogether, five aspirations of the brain abscess in a period of 25 days yielded a combined

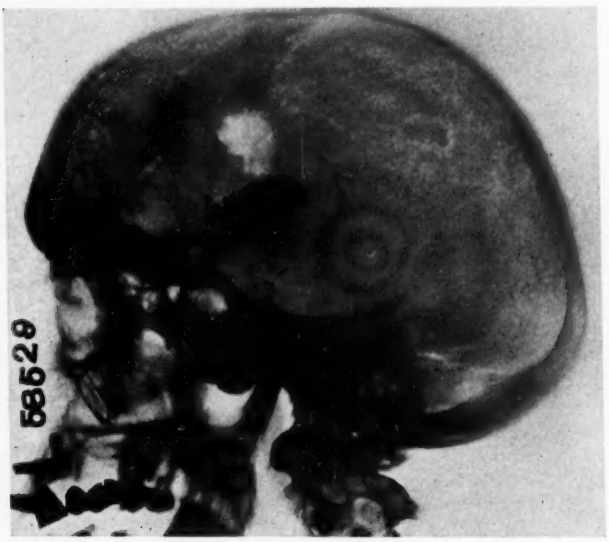

FIG. 2. Lateral view of the abscess cavity after the injection of lipiodol.

total of 123 cc. of pus which at each aspiration was thicker, and each time the abscess capsule was more resistant to penetration. The last aspiration yielded less than 5 cc. At each aspiration penicillin was instilled into the abscess cavity, to a total of 300,000 units used locally, and making the overall total penicillin 3,780,000 units.

Course. After December 13 (the 25th hospital day) the patient's condition improved steadily. He became constantly alert and reacquired his ability to understand written and spoken English, to speak connectedly and correctly, and to think spontaneously and normally. He hesitated over an occasional word. He had no weakness of his extremities. Electroencephalography showed his left temporal focus to be greatly diminished. At no time did he have papilledema or a *definite* visual field defect. His vision was excellent. Lumbar puncture showed no evidence of activity in the spinal fluid. He had no pulmonary complaints and physical examination of the chest was negative. The x-ray examination showed only slight residual density and bleb formation in the left lower lobe of the lung.

A pneumoencephalogram carried out prior to the patient's discharge from the hospital disclosed moderately dilated ventricles with a slight shift to the right.

COMMENT

The patient had no history of foul sputum and there is some uncertainty whether the

pulmonary suppuration found at thoracotomy was putrid. When he was first seen at this hospital however, the drainage from the chest sinus had a foul odor. The pus aspirated from the brain abscess was without odor. This was the first time that we had encountered odorless pus in operating on this type of abscess. We attributed the absence of odor to the bacteriostatic effect of penicillin. It is known to have this effect in the lung when used in the treatment of pulmonary abscess.[5]

Nor are we certain that this patient is cured. The pneumoencephalogram shows a ventricular shift. This is accounted for by the relatively thick capsule that remained. In view of the fact that the dominant hemisphere is involved it was believed wisest to leave it undisturbed if the patient remains symptom free. A similar course was followed by Wright[8] in a like situation.

If we disregard for the moment any direct effect the penicillin injected into the abscess cavity may have had, it is possible that in brain abscesses metastatic from suppurative pleuropulmonary disease, penicillin will be of value in controlling the early spreading cerebritis. In so doing the patient may live a sufficient time to encapsulate the purulent focus, permitting successful surgical interference.

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A SPECIAL SELF-RETAINING RETRACTOR FOR USE IN THE INTERLAMINAR APPROACH TO HERNIAS OF THE INTERVERTEBRAL DISC

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Operations for removal of hernias of the intervertebral disc have been greatly simplified in the past several years. Modifications in technique and the introduction of special instruments have aided in this simplification.

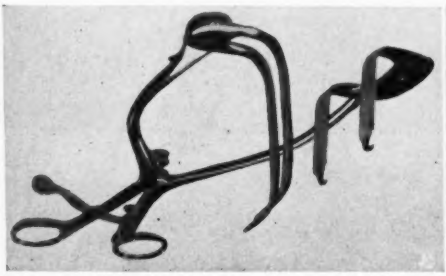

Fig. 1.

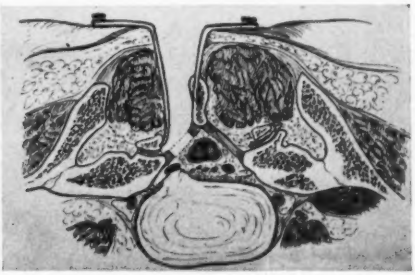

Fig. 2.

The retractor herein described (Fig. 1) is used with the patient in the modified kidney position with the side of pain uppermost, the lower knee forcibly flexed upon the patient's chest and the table broken slightly. The patient is held in this position with a wide band of adhesive passing up over the buttocks and across the patient to include the under or flexed knee.

The retractor permits adequate exposure of one or two interlaminar spaces through a 6-cm. skin incision. It is designed so that one blade hooks upon the interspinous ligaments and the other blade extends more deeply to retract the lumbar muscles (Fig. 2). The blades are interchangeable for varying depths.*

THE LATERAL POSITION FOR OPERATIONS IN THE CEREBELLOPONTINE ANGLE

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The purpose of the lateral position is to utilize gravity to effect retraction and thereby to minimize the trauma to the cerebellar hemisphere. This position serves effectively in patients who require section of the 5th, 8th, 9th or sensory portion of the 10th nerves. In these patients after the initial retraction, the retractor can usually be removed and good exposure is obtained even with the limited openings in the bone as described by Adson or by Dandy. In some cases of tumor of the 8th nerve adequate exposure is obtained without excision of the overlying cerebellar hemisphere. Exposure high in the angle at the incisura is better than it is with the patient in the prone position.

DESCRIPTION

The patient is laid on his side (Fig. 1) with his thighs and knees flexed in order to maintain

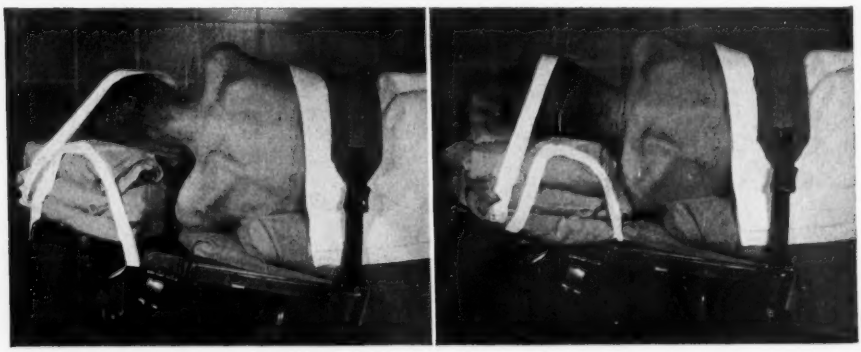

FIG. 1 (*left*). The patient is placed on the table in the lateral position with the neck flexed to afford better exposure.

FIG. 2 (*right*). The tapes fastening the sandbags to the head piece have been cut and the sandbags have been pushed backward and rotated so as to extend the neck for closure.

* This instrument is made by Edward Weck & Company, Inc., 135 Johnson Street, Brooklyn 1, New York.

the lateral position. A large pillow is placed between his legs. The patient rests on top of a series of folded blankets or a stretcher cover. These end just below the shoulder and relieve the excess pressure on the shoulder that would otherwise exist. The head is then taped to one or two sandbags. A space is allowed for the ear by permitting it to rest between two folded towels, in the center of which sufficient cotton is placed to elevate the head adequately on either side of the ear. The sandbags are shifted on the head piece to produce flexion of the neck. They are then taped to the head piece. When closure is started, these tapes can readily be cut and the sandbags and head slid backward in order to extend the neck and facilitate the closure (Fig. 2).

TRANSVENTRICULAR WOUNDS OF THE BRAIN

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A RECENT series of 342 penetrating brain wounds collected during the African, Sicilian and Western European campaigns drew attention to the technical difficulties peculiar to the repair of trans- and intraventricular penetrations.[4] This group of patients exhibited a clear-cut clinico-pathologic pattern. They constitute a challenge and are of unusual interest to the neurologic surgeon.

The bad prognosis of ventricular wounds has been noted by Cushing;[3] in 16 cases in which the projectile penetrated or traversed the ventricles there were no recoveries and the condition in most instances was a post-mortem finding. Other communications have not encompassed various types or locations of wounds, nor have they taken into consideration the picture presented and the treatment necessary for such wounds.[1,2,5] In the personal series referred to above this was attempted, and attention was drawn to prognosis as to life, dependent upon the areas of brain involved. The surgical problem presented by ventricular penetrations will be discussed in detail in this communication.

The patients reported here were all operated upon by the author or by an assistant under the direct supervision of the author (Table 1).

PATHOLOGY

Ventricular wounds are caused by missiles lodging in or passing through any part of the ventricular system. Lesions including the aqueduct and the 4th ventricle were not seen for obvious reasons, but the lateral ventricles, commonly, and the third ventricle, rarely, were involved. The missile was usually small, sometimes of match-head size. These constitute a group of wounds technically difficult to repair, but causing a minimal amount of ependymal damage and offering the best prognosis.

The pathologic study of the brains suspected of harboring a ventricular wound was facilitated at necropsy by laying open the ventricular system by sagittal section of each cerebral hemisphere.

Missiles entering from any part of the cerebrum caused little brain damage throughout the course of their tract until the ventricle was pierced or the missile stopped. An explosive effect was noted at the end of the missile tract. Much damage, maceration of brain tissue and old bleeding was found there. The damage to the ventricle varied with the size of the missile. The ependyma was softened and macerated at the point of entrance and exit. The ventricle itself contained debris, and, if bleeding had occurred,

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a sizable amount of old clotted blood. The bleeding was extensive if the choroid plexus had been struck. Those brains studied at necropsy, after suitable fixation, revealed the limits of damage necessary to cause death. The entire ventricular system, including the 4th ventricle, was filled with clotted blood and the ventricle involved was filled with old blood, macerated brain and ependymal tissue. The foramen of Monro was occluded in many such brains seen at necropsy. Those brains studied at surgery exhibited every gradation of the above pathology. Surgery was aimed at preventing or relieving the above conditions.

Larger missiles caused greater damage. Maceration of more than one-third of the ventricular wall seemed incompatible with life. Clean amputation of a macerated ventricle and cerebral lobe, under direct vision, carried a better prognosis.

Those patients presenting an occluded foramen of Monro also revealed a dilatation of the ipsolateral ventricle. This was noted in injuries only 24 hours old.

The presence of diffuse brain damage, manifested by scattered petechial hemorrhages, depended upon the size of the missile and consequent force of the blow. Most of the wounds were caused by tiny missiles and the diffuse brain damage was slight. Indriven bone fragments rarely extended as deep as the ventricle and usually hemorrhage into the tract was slight.

A transventricular wound, which usually meant one extending beyond the midline, revealed marked pathology on the distal side of the ventricle, as well as within the ventricle. Here was seen the explosive effect of the stoppage of the missile; the area of brain maceration and old hemorrhage was usually extensive.

Three cases of ventriculitis, studied at necropsy, revealed the above pathology, plus an extensive softening of the ependyma of only the lateral ventricle involved. The foramen of Monro was occluded by debris in both. The ependyma was soft, friable and edematous and was covered with a thick layer of cellular debris. There was no concomitant meningeal pathologic change and the missile tract was clean.

SYMPTOMATOLOGY

Patients sustaining ventricular wounds exhibit the usual neurologic deficits contingent upon the brain structure damaged during the passage of the missile. The actual functional brain damage was slight in most cases because the missile was small. The patient was usually, therefore, conscious, alert and oriented, and demonstrated only minimal neurologic signs.

A persistent, abnormally high temperature was a consistent finding in ventricular wounds. The temperature usually ascended as the patient's general condition declined. A temperature of 106°–107° was not uncommon and vigorous means to combat this were necessary. Hyperthermia may be attributed to the leakage of blood into the 3rd ventricle and stimulation of the paraventricular nuclei of the hypothalamus.

The important clinical aspect of such a wound is the rapid deterioration of the patient. The tiny wound of entrance and the neurologic picture, which is grossly negative except for slight apathy or haziness, might be noted and

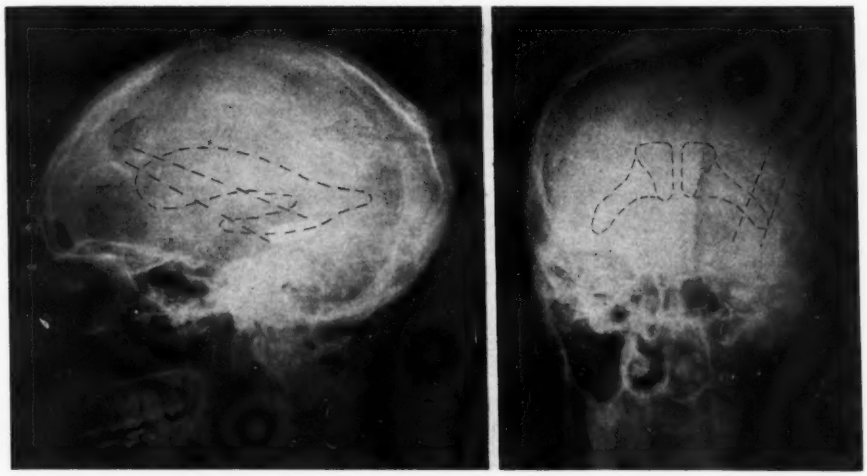

FIG. 1. Case 1.

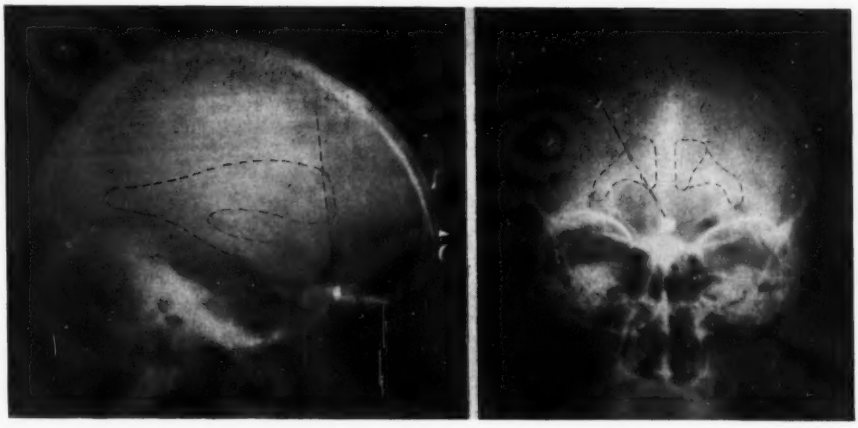

FIG. 2. Case 2.

ignored. The patient commonly becomes comatose or even moribund, however, within a period of eight to twelve hours. This is the typical picture of trans- or intraventricular wounds.

X-rays provide the diagnostic criteria necessary for the recognition of this type of wound. A small, metallic foreign body which crosses the mid-

line or extends in an anterior-posterior or posterior-anterior direction, or passes from the vertex to the base, usually courses into or through a ventricle. The path of the larger fragments is obvious (Figs. 1–3).

The diagnosis is established by the combination of rapid deterioration of a patient exhibiting a small penetrating brain wound, associated with hyperthermia, plus the radiographic finding of an intracranial missile which probably traversed a ventricle. Other diagnostic procedures are of no importance. A lumbar puncture is unnecessary and serves no useful purpose. There is neither time nor necessity for air studies. It should be noted, however, that on three occasions a traumatic ventriculogram made the diagnosis obvious.

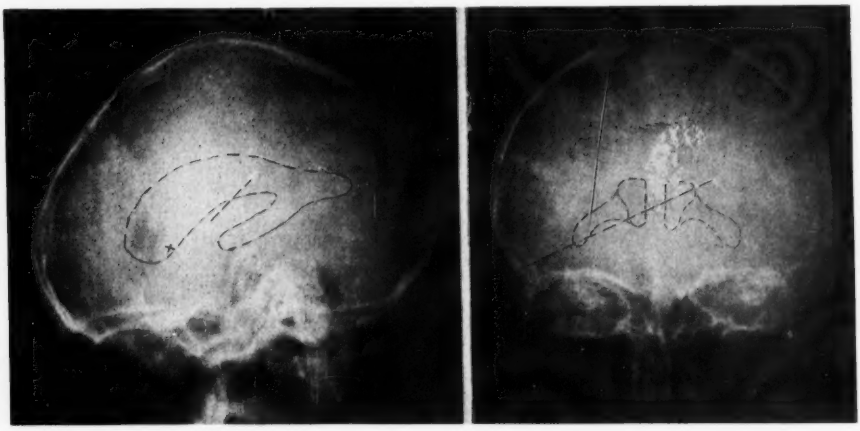

FIG. 3. Case 3. "X" indicates air in the ventricle.

TREATMENT

The patient must be operated upon immediately once the diagnosis is established. Rapid deterioration leads quickly to death unless the pathologic physiology is relieved. This is a neurosurgical emergency wherein a life may be saved if prompt and rational treatment is instituted. The prognosis is extremely bad once deterioration has developed to the point of coma.

The entrance wound is explored in the usual manner. The bony defect is enlarged with a rongeur until the margins of the dural rent are revealed. The small missile tract is found with a brain needle, which also localizes indriven bone fragments. These, and macerated brain tissue, are removed by suction and irrigation, through either the brain needle or a long, glass aspirator, until the ventricle is reached.

The ventricle is entered with the brain needle and as much blood as possible is aspirated. Blood clot, if present, will be seen clinging to the needle. The presence of clotted blood requires the introduction of a long glass aspirator into the ventricle. Alternate irrigation through the brain needle and suction through the aspirator will remove most of the clot and debris. This is continued until the return flow is clear. If bleeding persists, it is controlled with warm

saline solution. An attempt should be made to open the foramen of Monro if it is occluded by debris. The opposite ventricle should be entered through a separate burr hole, and saline gently forced from the intact ventricle through the occluded foramen into the damaged ventricle, where it is aspirated. This must be done gently. The saline must be no warmer than 100°F. These two precautions must be observed, otherwise edema of the tissue will occur and the purpose be defeated.

The transventricular missile tract can be located by a brain needle and followed through the ventricle by means of a long, glass aspirator. The danger of choroid plexus damage and bleeding necessitates gentle suction while the tube is in the ventricle. Finally, when hemostasis is complete, 50 per cent penicillin solution (20,000 units) is instilled into the ventricle. This has been non-irritating to the ependyma and has been used routinely. The dura is then closed and the scalp sutured in layers.

Postoperatively, increased intracranial pressure may be controlled either by contralatera

TABLE 1

Morbidity and mortality of 100 ventricular wounds

Type of Wound Penetrating or Traversing Ventricle	Number of Patients	Recovered	Infections				Deaths		Postop. Mortality Rate	Over-all Mortality Rate*	Incidence of Infection*
			Scalp	Meningitis	Ventriculitis	Abscess	Preop.	Postop.			
Deep, narrow missile tract	28	18	1	0	1 (d)	0	3	7	28.0%	35.7%	8.0%
Larger (1 cm. or more) missile tract	26	12	0	1(cured)	1 (d)	0	7	7	36.8%	53.8%	10.5%
Extensive brain damage	46	21	1	2	1 (d)	0	13	12	36.3%	54.3%	9.1%
Totals	100	51	2	3	3	0	23	26	33.7%	49.0%	10.3%

* Incidence of infection concerns only postoperative patients. Over-all mortality rate includes all patients reaching the neurosurgeon alive.

ventricular taps or cautious lumbar punctures. Ventricular puncture seems preferable. Penicillin is instilled at the termination of either procedure.

The necessary operative treatment of larger missile tracts can be effected under direct vision, but the mortality rate is in direct proportion to the ventricular damage. Intraventricular foreign bodies, if easily accessible, may be removed under direct vision. It is advisable to leave them *in situ* if their removal entails destruction of a sizable amount of ependyma. Such delay allows the ventricle to dilate. This facilitates the subsequent removal of the foreign body. The patient's general condition will probably improve in the interim. There is no objection, at this stage, to leaving a small, metallic foreign body in the wall of the ventricle, if it does not occlude the foramen and if it is not easily accessible.

Increased experience allowed the objectives of the operation to be accomplished more frequently. Admittedly, blind aspiration of a narrow missile tract is hazardous, but if one is cognizant of the dangers and prepared to deal with them, the results justify the risks. The missile tract is usually too narrow to admit lighted brain retractors safely. As an alternative to the blind method described above, the use of a ventriculoscope is suggested. Such an instrument would permit the operation to be performed under direct vision. This should prevent damage to the choroid plexus and

allow inspection of the interior of the ventricle. Metallic foreign bodies could be removed and instrumentation accomplished.

PROGNOSIS

The over-all mortality rate of penetrating brain wounds in an earlier communication was found to be 25 per cent. Ventriculitis, widespread destruction of the ependyma, or the filling of the entire ventricular system with blood clot, is followed by death. For this reason a prohibitive mortality rate had been anticipated. In this series the actual mortality rate from, and incidence of infection in, ventricular wounds is seen in Table 1.

SUMMARY

1. Because of their repetitious nature the author has attempted to classify penetrating brain wounds and has presented here one such category, that of the transventricular brain wound.

2. Pathologic and clinical peculiarities of such wounds are described.

3. Technical details and the results of reparative surgery are discussed.

4. Value of a ventriculoscope in such surgery is suggested.

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EXTENSIVE BRAIN WOUNDS

ANALYSIS OF 159 CASES OCCURRING IN A SERIES OF 342 PENETRATING WAR WOUNDS OF THE BRAIN

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A SERIES of 342 penetrating brain wounds collected during the African, Sicilian and Western European campaigns, has recently been reported. An attempt was made to classify brain wounds as to type, location, treatment required and prognosis as to life dependent upon brain areas involved. These wounds assumed a repetitious pattern and it became possible to define broad principles pertaining to each group.[5]

Two categories particularly challenged the knowledge and skill of the neurologic surgeon. One was the trans- or intraventricular wound and the other was that severe wound causing extensive brain damage. The first has been described in detail[6] and it is desired here to portray the peculiarities of more gross brain wounds. An inordinate number of patients suffering extensive brain damage has been included in the larger series referred to above. Casual acceptance of this fact represents a distorted cross section of the severity of intracranial war wounds. The reason for such distortion is that most of these severely wounded patients were seen and operated upon in consultation. No attempt is made at a long-term study of psychiatric evaluation, late infection, epilepsy or eventual social worth. Such an analysis will take years and is best carried out by the proper agencies after a suitable follow-up period.

Battle wounds of the brain are far removed from civilian neurosurgical problems. It seems reasonable, however, to expect a gain in knowledge of technical brain surgery through such an unfortunate means. New approaches have been evolved and new techniques devised to meet the complex and unexpected demands of patients receiving penetrating brain wounds.

ETIOLOGY

Extensive brain damage was caused by large shell fragments penetrating the brain, glancing off or through the skull and brain, or perforating the brain. Wounds caused by small-arms fire constituted only a small percentage of the cases seen. Machine gun bullets of .30 and .50 calibre caused a tremendous amount of damage. Pieces of helmet may become imbedded in the skull or carried into the brain by the penetrating missile. Many wounds were of the gutter type, because of a prone position and the wearing of a helmet. Missiles were deflected from their course by helmet or skull to penetrate the shoulder, chest or back. Examples have been seen wherein the fragment

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struck the inside of the helmet and followed the curve of the helmet around the skull, making an exit on the other side. Study of the helmet will determine the path of the bullet. A missile entered the mastoid region of the scalp, on one occasion, tangential to the curve of the skull. It remained between the skull and scalp and was deflected to emerge from the frontal region, only nicking the orbital ridge as it passed. The skull and brain were spared and the scalp showed only an entrance and an exit wound.

The most common agent was that of a fairly large piece of high explosive shell fragment. During the passage through bone and brain it caused a great amount of local maceration of brain tissue. A marked degree of diffuse brain damage was present because of the powerful striking force.

PATHOLOGY

It is difficult to separate those instances of extensive brain damage from those of a lesser degree. A match-head sized missile may cause little local damage and yet, because of vital centers involved, mean death. A large missile, causing tremendous local damage to a non-vital area of the brain, may spare life and the patient recover quickly.

It is emphasized that extensive brain damage is not coincident with death. The discussion must include those patients in whom a remarkable amount of brain tissue has been destroyed and removed, and those in whom concomitant diffuse brain damage has been extensive. To express this quantity mathematically seems difficult. The author hopes only to point out that a deeply comatose patient with extruding, macerated, cerebral tissue is amenable to surgery and that many of them can be saved.

This analysis is confined to those patients in whom a cerebral lobe, or a major portion of a cerebral lobe, has been destroyed; perforating wounds of the brain; and very large missile tracts penetrating deeply into or through the brain. Almost all of them represent transventricular wounds as well.

The diffuse brain damage, at necropsy, was most marked in a gutter type of brain wound, but was well demonstrated in all brains where the missile was large and the striking force great.

Multiple petechial hemorrhages were grouped throughout both the white and the gray matter. They extended, in severe cases, throughout the midbrain, pons and even the cerebellum. The diffuse pathology was evenly distributed in brains portraying great local brain damage. The contrecoup effect was usually notable in instances wherein the wave of force was transmitted through the skull and the brain but with little or no local damage. An actual sine wave of force, of small frequency, was noted throughout the brain in some cases. Maxillo-facial wounds presented, many times, local basilar areas of contusion accompanied by diffuse brain damage.

Subdural bleeding obviously accompanied any dural penetration, as did subarachnoid and intracerebral bleeding. The surgical importance, since the bleeding had always stopped, was secondary to the repair of the brain wound.

The brain tissue was macerated, softened and hemorrhagic. The explosive action of the stopping of the missile was usually marked and extensive softening and hemorrhage at the end of the missile tract was the rule.

Gutter wounds, of great severity, were common. A large macerated area of the brain was secondary to the passage of the missile through the cranial cavity. Large indriven bone fragments and the actual force of the blow to the skull caused more widespread damage. It was felt on two occasions that a hemorrhagic, macerated occipital lobe was compressing the brain stem through the incisura of the tentorium. Respiration ceased in one case, and in another virtually ceased. Life was restored in both instances by swift resection of the already macerated occipital lobes. The amount of hemorrhage into that critical location had been extreme. Such a condition was not recognized at any necropsy, but the surgical pathology seemed apparent in the two procedures described.

Large venous sinuses were commonly torn or lacerated by bone or missile. They had usually thrombosed by the time the patients arrived at surgery. Large cerebral arteries and veins were no exception. Hemorrhage was never found to be the cause of death except in those patients wherein gross ventricular bleeding had occurred.

SYMPTOMATOLOGY

Signs and symptoms were dependent upon the structures damaged by the missile, and those involved by concomitant diffuse brain damage. Various cortical, thalamic and pyramidal signs were elicited; the visual pathways were commonly interrupted, and injuries to the basal ganglia caused the expected abnormalities of tonus. Cranial nerves, except for the 7th, were rarely involved. Midbrain signs, such as hemiballismus and 3rd nerve paralysis, were seen fairly frequently. Hypothalamic lesions were reflected by autonomic and temperature changes. Cerebellar wounds revealed the usual hemispheric picture of extremity ataxia and asynergia. Medullary damage was not seen at operation.

The usual picture was that of a deeply comatose patient, presenting a rapid pulse and stertorous respirations, plus a low blood pressure. Macerated brain extruding through a large skull defect was common. Neurologic findings, difficult to evaluate because of coma, were only indicative of the area of brain destroyed, already estimated visually. Previous conceptions, such as the location of the arm area on the motor strip, oculomotor cortical center, and quadriplegia due to thrombosis in the posterior third of the sagittal sinus, were questioned but deserve much greater postoperative study.

Rarely did the classical signs of a cerebral wound, such as high blood pressure and slow full pulse, present themselves. The condition seen was that of a cerebral insult or shock.

Roentgenographic study was carried out when the patient's vital signs

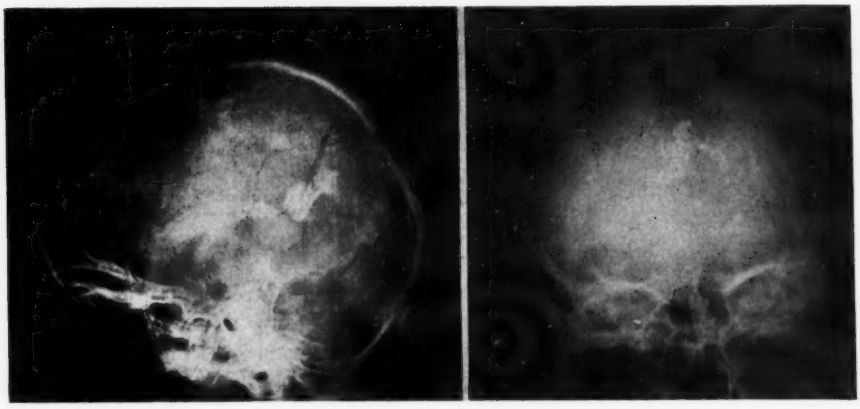

FIG. 1. Severe occipito-parietal gutter wound. Recovery.

stabilized. X-ray facilities were lacking in the very early days on the Normandy beach-head. This lack was not felt so keenly as expected. Radiographic study revealed the type of wound and usually the type, location and size of the missile. It also allowed prognostication as to structures involved and life or death based upon such factors (Figs. 1–4).

FIG. 2. Poor X-ray of a perforating brain wound. Recovery.

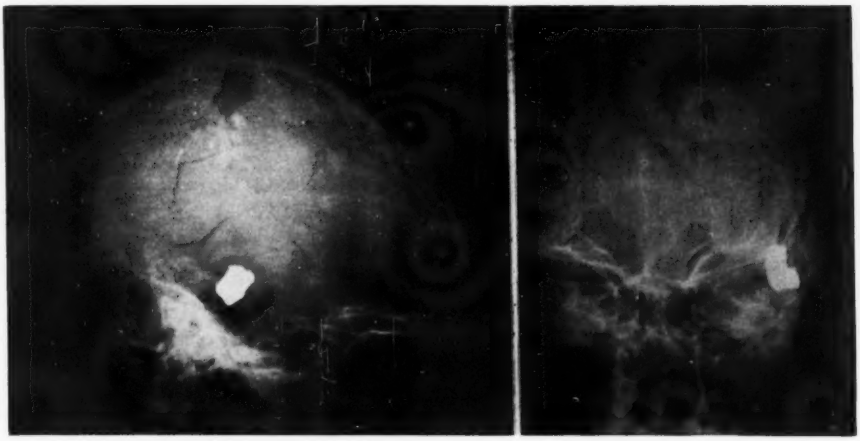

FIG. 3. Extensive parieto-temporal damage. Recovery.

TREATMENT

The essential wait for stabilization of vital signs has been described.[5] The patient presenting a severe intracranial wound during this period, received the usual supportive treatment necessary to combat the cerebral insult. There was no substitute for whole blood, although plasma contributed to recovery. Oxygen was used freely, as was caffeine in small, repeated doses. The respiratory tree was kept clear by aspiration and the

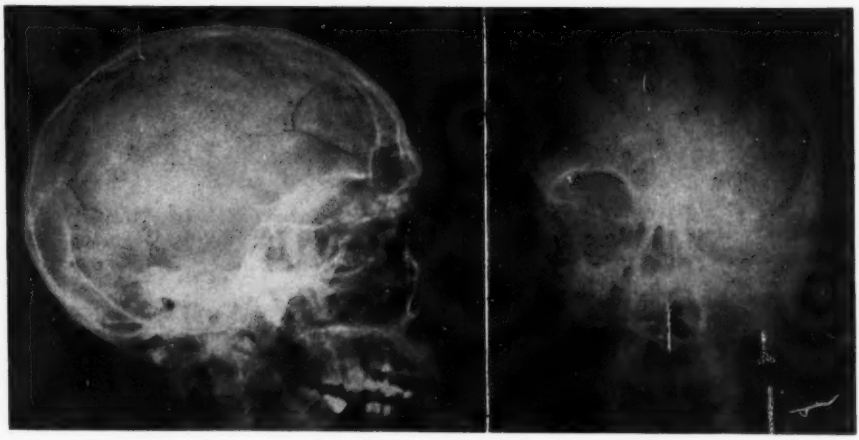

FIG. 4. Severe left frontal lobe, sinus, orbit wound necessitating a frontal lobectomy. Recovery.

patient was kept warm. Paraldehyde was used for restlessness. Usually, within 2 to 12 hours, the vital signs stabilized and the patient reached the optimal level for surgery. Operation must be effected at this time. Once this peak has passed, his chances for survival are lessened. He is given the opportunity of surgery if he shows no signs of improving after an adequate time lag to await the peak. This is done with the full realization of the probable outcome, but it seems mandatory to offer the benefit of surgery even to the moribund. There is no objection to waiting even 48 hours for stabilization of vital signs if improvement is noted. That the above plan is a meritorious practice is shown by the fact that some 50 per cent of these apparently doomed patients survive.

Sodium pentothal, supplemented by local procaine infiltration of the scalp, was the usual anesthetic agent. The more judicious choice, in gravely wounded and critically ill patients, seemed to be local infiltration of the scalp and paraldehyde, 4 cc. intramuscularly, for sedation. Since a transfusion was usually given during the operation, pentothal could be administered quickly if needed. Atropine was given preoperatively with this in mind. Choice of anesthetic agents wherein further depression of vital centers may precipitate death, is a matter of judgement. Rarely did pentothal seem contraindicated, but the patient requiring fast, life-saving surgery, and with depressed vital functions, needs little anesthesia beyond sedation and local infiltration.

The actual technique of traumatic, reparative, neurologic surgery has been outlined previously.[2,3,4,5,7] The principles involved in operating upon patients suffering extensive brain damage remained the same. Macerated brain is resected to healthy margins, indriven bone fragments are removed and complete hemostasis is assured. Sulfanilamide and penicillin powder are dusted into the wound, the dura is closed and the scalp closed in layers. The repair must be primary and definitive and must be early to obviate later infection.

The above principles led logically to the completion of a traumatic amputation of one or more lobes of the brain, a "lobectomy necessitans." It is emphasized that viable, functional brain tissue was spared at all times and the procedure does not represent an elective resection. It was carried out with the aspirator, electro-coagulator and lighted brain retractors through the original traumatic defect. Hemostasis was not a serious problem, the vessels usually being thrombosed. It is noteworthy that the appearance of an extensive brain wound is misleading. The large hemorrhagic mass of material, assumed to be cerebral matter, extruding from a large cranial defect, is almost entirely blood clot.

The dural defects are large in such extensive wounds. These are always closed by either a periosteal, temporal fascia or fascia lata graft. The graft is usually clipped in place with Cushing silver clips. Sewing, because of cramped quarters, is impractical and laborious.

The appearance of ventricular fluid in the depths of such a wound is not

a sign to desist. Rather, the macerated brain must still be cleaned out, ventricular damage repaired and absolute hemostasis effected. The latter is imperative. The clean amputation of the tip of a ventricle is not incompatible with life.

Some patients had such extensive wounds that more than one lobe was badly mangled. Adequate resection in such cases meant a bilateral lobectomy. These wounds were usually frontal. The patients usually survived the trauma and subsequent operation, although their residual vegetative state was pathetic.

Posterior and anterior cerebral, as well as anterior communicating arteries, of necessity, were frequently clipped. The only untoward effect noted followed occlusion of both anterior cerebral arteries and consequent bilateral frontal lobectomy. This resulted in a low level of consciousness. The middle cerebral was not occluded proximal to its basal ganglia[3] branches. Observations as to its necessity for life are lacking. It was clipped frequently distal to the basal ganglia branches and had no primary detrimental effect on the recovery of the patient.

Occlusion of the internal carotid artery was seen in four patients. This was due to damage to the vessel wall and subsequent clot formation. All but one followed the internal carotid syndrome of progressive coma, hemiplegia and death. Necropsy revealed massive softening of the ipsolateral cerebral hemisphere. The one patient that recovered did so slowly, but remained aphasic, hemiplegic and hemianopic.

Penetration into, and hemorrhage from, the large venous sinuses was seen frequently. The entire torcular had been destroyed in two instances. These had all thrombosed by the time surgery was attempted. Ligation of a sinus was never accomplished, muscle stamps being sufficient to stop the flow of blood. On one patient, memorable because of the technical difficulties involved, operation was attempted twice. The first was carried out through the original defect, by-passing the torn torcular to clean out a large, midline, occipital, missile tract down to the midbrain. Furious hemorrhage, controlled with great difficulty, met this attempt. The wound was closed and 36 hours later an approach lateral to the tract was attempted. Again, the torn sinus ends bled furiously. The operation, of necessity, ceased, to await the inevitable abscess formation and thorough thrombosis of the sinuses. The patient's condition was excellent. This seemed the better judgement, since the abscess could be more easily treated than a primary repair effected.

Patients presenting perforating wounds of the brain, who survived the trip to the neurosurgeon, usually withstood operation well. The cleaning of the tract was a comparatively simple procedure. Irrigation through the entrance, and then through the exit, wound, adequately removed the macerated brain. The usually large tract could be followed down and resected easily and safely by means of the suction. The resultant vegetative and paralytic state was lamentable.

An interesting group of patients was that exhibiting a usually inaccessible

entrance wound near the base of the skull. The missile may have passed through the brain to lodge subcortically near the vertex. Here accurate X-rays were of vital importance. A foreign body locator was not available. A burr hole was placed over the foreign body. The overlying subdural clot was evacuated and a small cortical incision made over the foreign body. This was located with the brain needle and removed. The tract was then accessible for adequate cleansing and constituted no problem.

Extensive cerebellar damage was evident in only four patients. A resection of damaged cerebellar hemisphere was carried out in each instance. They all recovered, but at the time of their evacuation, 5 to 10 days later, portrayed a neo-cerebellar syndrome.

Combined extensive brain wounds and spinal cord wounds were seen and operated upon three times. One patient lost his left frontal lobe, the tip of his right frontal lobe, the right frontal sinus and posterior orbital plate and the right eye. His spinal cord lesion was incomplete and laminectomy caused a complete return of function. His mental status, when discharged, was good. The only gross defect seemed to be a lessening of inhibitions which was not marked. He was a socially acceptable individual and the result of surgery seemed satisfactory. One other patient recovered from his right frontal lobectomy. Laminectomy revealed an anatomically intact spinal cord but he had no return of function in his legs at time of evacuation 15 days later. The other patient died postoperatively from a severe transventricular wound. His spinal cord had been transected.

It seems evident that a well trained, smoothly functioning neurosurgical team is of paramount importance if such major procedures are to be efficiently carried out. This consists of an instrument nurse, anesthetist, two medical technicians and an able surgeon assistant.

Sulfanilamide and penicillin powder were used locally in all wounds and penicillin solution instilled in each deep missile tract or ventricular wound. The author gives full credit to both drugs, and to swift evacuation of the patient to the neurologic surgeon, for the marked decrease in mortality and morbidity rates. He feels strongly that penicillin is of great value in preventing and treating cerebral infections. The reduction of infection incidence from 37.5 per cent in the last war to the present low rate is due to swift evacuation and penicillin. It seems more efficacious, locally, than sulfanilamide. Its effect on actual infection, when used intrathecally, is dramatic.

Careful observation of the patient was carried out postoperatively. The head was elevated to promote cerebral venous drainage. The respiratory tree was kept clean by aspiration. Oxygen, caffeine and whole blood were used when indicated. Cautious ventricular and lumbar punctures were used to combat cerebral edema. Fluid and caloric requirements were met, in the comatose patient, through a Levine tube. Sulfadiazine and penicillin therapy was carried out routinely. Intrathecal or intraventricular penicillin

was given to each infected, or potentially infected patient. Paraldehyde was used for restlessness.

PROGNOSIS

The over-all mortality rate of wounded during the Western European campaign was roughly 3 per cent. The operative mortality rate of penetrating brain wounds, reported by the author, was 13 per cent.[5] The operative mortality rate of this series of patients suffering extensive brain damage

TABLE 1. *Analysis of extensive brain wounds*

	Type of Wound	Total	Operated	Deaths		Recovery to Normal (Socially Useful)	Infection*	Over-all Mortality Rate	Postop. Mortality Rate	Incidence of Infection*
				Preop.	Postop.					
"Lobectomy necessitans"	Extensive damage (over 2-cm. tract)	38	32	6	6	13	15	31.5%	18.7%	46.7%
	Frontal	41	36	5	5	22	5	26.8%	13.8%	13.8%
	Temporal	8	8	0	5	0	1	62.5%	62.5%	12.5%
	Occipital	24	17	7	5	4	6	50.0%	29.4%	34.0%
	Parietal	14	10	4	3	2	6	50.0%	30.0%	60.0%
	Bilateral frontal	4	4	0	0	2	0	0.0%	0.0%	0.0%
	Bilateral occipital	3	2	1	1	0	0	66.6%	50.0%	0.0%
	Perforating	9	7	2	2	3	0	44.4%	28.5%	0.0%
	Cerebellar	5	4	1	0	4	0	20.0%	0.0%	0.0%
	Midbrain	13	3	10	2	1	0	92.3%	66.6%	0.0%
	Grand total	159	123	36	29	51	33	40.8%	23.6%	26.8%

* Almost all wounds were ventricular as well. There were 24 infections—16 abscesses and 8 fungi—present upon arrival. The infection incidence is exaggerated here because of delay in surgery in the African campaign. A true infection incidence is arrived at elsewhere.[5] In the Western European campaign 2 brain abscesses, 7 cases of meningitis, and 7 scalp infections were seen. Of the patients with these extensive brain wounds 42 per cent were socially acceptable after a 10-day observation period. They were not hemiplegic, aphasic or blind. Their mental content was grossly normal.

is 23.6 per cent (Table 1). Mortality rate of penetrating brain wounds in the last war was 37.5 per cent, reported by Dr. Cushing. Ascroft,[1] in this war, reported a 20 per cent operative mortality rate and 25 per cent of those surviving became infected. The mortality rate of penetrating abdominal wounds in this war is approximately 21 per cent and of all compound fractures reaching a forward hospital, 5 per cent. Comparatively speaking, then, the patient receiving a severe brain wound has more chance to survive than has one with a penetrating abdominal wound. Distortion of mortality rate is obvious; it depends upon many factors. Distance from the front, rapidity of evacuation, type of wound operated on, and ability and judgement of the neurologic surgeon are contributory.

SUMMARY

1. The author has attempted to classify penetrating brain wounds as to type, location, pathologic and surgical peculiarities and prognosis. One such category, that of extensive brain damage, is exemplified in this group of 159 cases.

2. Pathologic and clinical peculiarities are described.

3. Necessary surgical technique and results therefrom are presented.

4. Comparison of results with over-all picture of war surgery is made.

5. Encouraging results are attributed to swift evacuation to the neurologic surgeon; primary, definitive repair; and sulfonamides and penicillin.

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SPASM OF THE INTERNAL CAROTID ARTERY

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IT HAS LONG been known that sudden occlusion of the internal carotid artery may produce enough interference with the blood supply of the cerebral hemisphere on the same side as to cause severe symptoms. However, the role of minor trauma to the internal carotid artery in the production of cerebral dysfunctions appears to have been given insufficient attention, although Makins[3] did raise the question whether spasm might be involved in cases of contusion of this vessel. The purpose of this report is to record a series of observations in which cerebral symptoms were produced from penetrating war wounds of the neck in which there was neither laceration nor thrombosis of the internal carotid artery.

CASES OF WOUNDS OF THE NECK

Case 1. This soldier suffered a bullet wound on 7 June 1944 at Normandy. The missile was a 0.30 calibre machine gun bullet, which entered the left cheek and came to rest just under the base of the skull, and just medial to the left mastoid process (Fig. 1). Little is

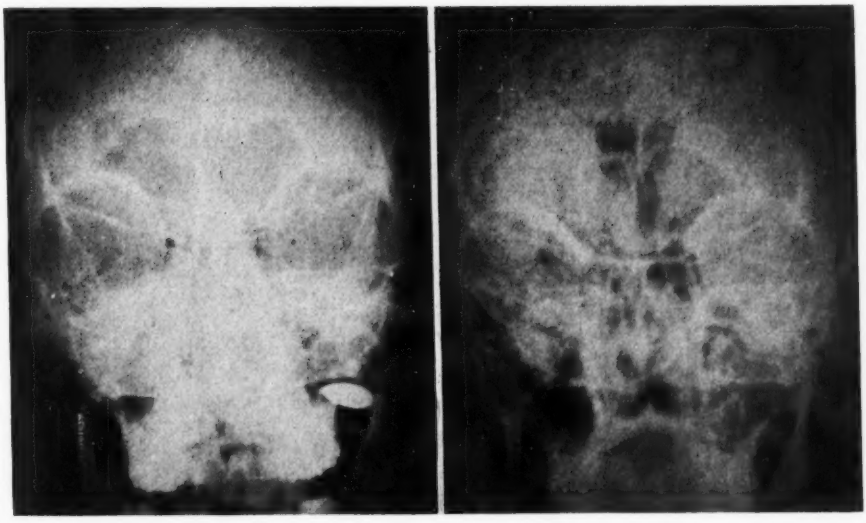

FIG. 1 (*left*). Case 1. Anteroposterior view of the skull.
FIG. 2 (*right*). Case 1. Encephalogram, anteroposterior view, showing dilatation of the 3rd ventricle and left lateral ventricle. The bullet has been removed.

known about the patient's condition for the first three days. He arrived in a fixed hospital in England on 10 June 1944. At this time he was very drowsy and apparently was suffering from

motor aphasia, although he responded with muscular movements to pain or noise. The blood pressure was 156/100, and the pulse rate 76. There were right hemiparesis, which was more marked in the upper limb, and transitory right ankle clonus. The corneal, pupillary, plantar and swallowing reflexes were normal. The right pupil was dilated, but responded to light. There was blood in the patient's mouth; the eardrums were normal. There was ecchymosis of the left side of the neck. The respiratory rate was 12.

X-ray films revealed the retained bullet just beneath the base of the skull and just medial to the left mastoid process, but on the films there was evidence of neither fracture of the skull nor intracranial foreign body (Fig. 1). Lumbar puncture revealed clear and colorless fluid under pressure of 300 mm. of water. On unilateral jugular compression and release on each side, there was prompt rise of spinal fluid pressure to 400 mm. and a prompt fall. The patient seemed brighter following lumbar puncture. For a few hours, the paresis of the right arm—especially the fingers—seemed to increase, and a tentative diagnosis of "intracranial hemorrhage (possibly epidural)" was made. However, within another few hours the respiratory rate increased to 20, the paresis of the right upper limb diminished, and the patient seemed less drowsy.

On 11 June 1944 the bullet was removed, but the internal carotid artery was not carefully examined. In the course of the next two weeks, the patient's general condition gradually improved so that he began to talk and say a few words. By 18 July 1944 the patient had regained moderate speech, and was able to take care of himself on the ward. On this date an air encephalogram was made. The spinal fluid contained 45 mg. total protein per 100 cc. The film (Fig. 2) revealed slight dilatation of the left lateral ventricle and of the third ventricle.

In summary, a "near miss" of the left internal carotid artery caused aphasia, right hemiplegia, increased intracranial pressure and residual left ventricular dilatation.

Case 2. This soldier was wounded in action in France on 23 June 1944. He suffered a perforating wound due to a small missile of unknown type. The missile entered the left cheek, caused a comminuted fracture of the left side of the mandible near the angle of the jaw, and left the patient's body from the right side of the neck. There was no fracture of the skull. The patient suffered immediate right hemiplegia, aphasia and respiratory difficulty. A tracheotomy was performed at a field hospital.

On 7 July 1944, the patient came under the care of the author in a fixed hospital in England. At that time examination revealed restlessness, aphasia, flaccid right hemiplegia, slight hyperactivity of the right tendon reflexes and the presence of Babinski's sign on the right. The small wound in the posteroinferior portion of the left cheek and on the right side of the neck were healed. The tracheotomy wound was healing. For a few days the patient could not phonate, but the ability to make sounds soon returned although speech did not return for a few weeks.

On 16 July 1944, encephalography was carried out and revealed considerable dilatation of the left lateral ventricle and of the third ventricle and slight dilatation of the right lateral ventricle (Fig. 3). The subarachnoid markings were normal. Cerebral arteriography was carried out on both right and left sides on 7 August 1944. The middle and anterior cerebral arteries and their branches on the left side were smaller than those on the right. Around 15 August 1944 the patient began to say a few words and there was slight return of strength of the right limbs, more in the lower than the upper.

In summary, a "near miss" of the left internal carotid artery caused aphasia, right hemiplegia, dilatation of the lateral ventricles more on the left than on the right, and diminution in calibre of the left middle and anterior cerebral arteries.

Case 3. A soldier suffered a penetrating wound on the right side of the neck 17 July 1944 and had immediate left hemiplegia. When he was examined at a fixed hospital 20 July 1944, a metallic fragment less than 1 cm. in diameter was found in the soft tissues of the neck anterolateral to and at the level of the 5th vertebra. At this time there was no clinically demonstrable residuum of the hemiplegia.

CASE OF A BLUNT HEAD INJURY

Case 4. This soldier fell off a truck at 3:00 o'clock on the morning of 22 June 1944. He was unconscious for a short time but soon regained responsiveness, although he remained

FIG. 3. Case 2. Encephalogram, anteroposterior view, showing generalized ventricular dilatation.

disoriented. There was bleeding from the left ear but no laceration of the scalp. In the next three hours he became progressively less responsive. At 6:00 o'clock he was in a deep coma, had stertorous breathing and episodes of decerebrate rigidity. His left pupil was greatly dilated and did not respond to light. Both Babinski and Hoffmann signs were present on each side. An X-ray film revealed a fracture of the skull in the left temporoparietal area extending across the posterior division of the middle meningeal artery.

At 7:30 o'clock, that is, 4½ hours after the injury, an emergency left temporal craniotomy was performed without anesthesia. An extradural blood clot, 2.5 cm. deep and about 7 cm. in diameter, was evacuated and the bleeding from the meningeal vessels was controlled. There was immediate improvement in the size and reactivity of the left pupil so that these were normal within 15 minutes after the removal of the clot. However, the patient failed to regain consciousness. His rectal temperature was 103.6°F. but later responded to cooling of the body. The blood pressure remained normal and there were no postoperative episodes of decerebrate rigidity. However, the pulse rate and respiratory rate remained high and the patient died 36 hours after the injury.

Pathologic Findings. Gross. A complete autopsy was performed and revealed no visceral lesion except bilateral pulmonary edema (weight of right lung 1110 gm., weight of left lung 855 gm.). At the site of the operation there was a small amount of epidural blood, which was nowhere more than 1 cm. deep. The brain convolutions were markedly flattened and sections of the brain revealed dilatation of its blood vessels without hemorrhage. The fracture line extended into the base of the skull along the petrous portion of the temporal bone. The portion of the left internal carotid artery lying within the carotid canal and that portion immediately

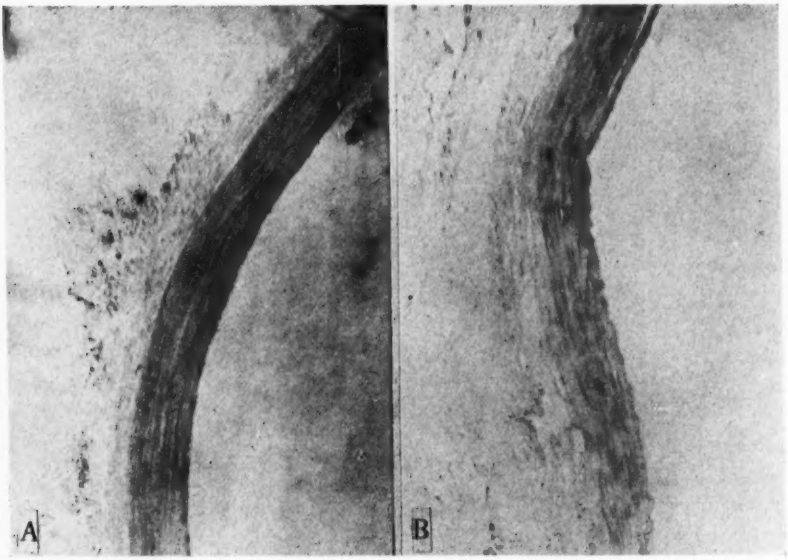

FIG. 4. Case 4. (A) Left internal carotid artery, described in the text. (B) Right internal carotid artery, normal control. Photomicrographs, × 100.

beyond its emergence from the canal were marked by hemorrhage into the wall of the vessel. The right internal carotid artery was normal.

Microscopic. Study of the sections of the left internal carotid artery revealed recent hemorrhage in two different areas of the outer portion of the adventitial connective tissue. There was no evidence of inflammatory reaction or organization. The outlines of the cells of the muscularis were obscure. The cells of the middle and outer thirds of the media were void of nuclei. The subintimal third of the media contained scattered nuclei, many of which were pyknotic. The intima was marked by a few scattered endothelial cells which were decreased in number and some of which were pyknotic. There was neither focal necrosis nor inflammatory reaction. The hemorrhage in the adventitia was probably terminal. Sections of the right internal carotid artery were used as controls (Fig. 4). These microscopic studies were made by Major Oscar Wollenman, M.C., A.U.S., and the findings are consistent with ischemic necrosis.

DISCUSSION

In Cases 1, 2 and 3 there were wounds of the neck with "near misses" of the internal carotid artery by missiles. There is no reason to believe that the internal carotid behaves differently from arteries of similar size supplying

the limbs in which the spasm is known to occur following such trauma. Cohen[1] has written of such lesions:

> The spasm is rarely maximal, the lumen being merely narrowed and the distal limb is rarely seriously endangered. It would appear reasonable to regard this form of spasm as consequent upon the sudden stretching of the vessel by lateral displacement due to the exploding force of the missile.

Because of the extreme susceptibility of the brain tissues to anoxia, a relatively minor impairment of its blood supply will yield profound dysfunction, thus differing from the situation in an extremity. In Cases 1, 2 and 3 there was evidence of neither laceration nor thrombosis of the carotid artery but very likely spasm took place.

Increased Intracranial Pressure. Moniz[4] has been impressed with intracranial hypertension following carotid thrombosis. He cites a case of severe traumatism of the head with so much traction on the carotid artery as to produce tears of the intima, which initiated a thrombotic process. A lesser amount of traction may cause spasm of the artery. The swelling of the brain in these cases is probably due to a combination of cerebral edema and congestion. The morphology and pathogenesis of these vascular disturbances have been characterized as vasoparalysis of the central nervous system.[6] In Case 1 intracranial pressure was found to be increased three days after the wounding. In Case 4 the autopsy revealed evidence of markedly increased intracranial pressure 36 hours after the injury.

Ventricular Dilatation. A recent study of traumatic dilatation of the cerebral ventricle indicates[5] that it may be well due to a generalized effect on the brain, although its microscopic pathology has not yet been identified. In Case 1 there was unilateral and in Case 2 bilateral dilatation of the lateral ventricle although there was no evidence of skull fracture in either case. It is, therefore, suggested that impairment of cerebral arterial circulation may be a significant factor in traumatic dilatation of the cerebral ventricle.

Neurosurgeons have recognized for some time the high frequency of death in cases of hemorrhage from the middle meningeal artery. It has been reasonable to suppose that death was due not to the hemorrhage itself but to the associated brain injury. In Case 4 an unsuspected lesion, ischemic necrosis of the internal carotid artery, was discovered at necropsy. In Fig. 3 of Holbourn's recent paper[2] on the mechanics of head injury, shear-strain due to a rotation in the coronal plane caused by a blow above the ear is seen to be maximal near the midline at the base of the skull. In other words, the nature of the blow that is most likely to cause a fracture of the skull across the meningeal vessels and extradural hemorrhage is the same as that in which the brain is most likely to pull on the circle of Willis and the internal carotid artery. As Cohen has shown, traction on an artery is one of the commonest causes of arterial spasm. In all fatal cases of head injury special attention should be devoted to both gross and microscopic study of the arteries at the base of the brain. As a matter of fact, abnormalities may not

be demonstrable in cases where death ensues promptly. The further demonstration of changes in cerebral arteries in head injury may await the more frequent use of cerebral arteriography. Wakeley and Orley[7] state:

> In mild cases of cerebral concussion or contusion arteriography reveals a contraction of the blood vessels. In grave cases and in the presence of cerebral tumefaction the blood vessels are flattened and fill incompletely owing to vascular paralysis and mechanical compression.

SUMMARY

There have been presented 4 cases of dysfunction of the brain which are considered to be due to relatively mild trauma of the internal carotid artery. The first three were cases of penetrating wounds of the neck without laceration or thrombosis of the artery or any evidence of direct head injury. The fourth case was a blunt head injury with a fracture of the skull and postmortem evidence of brain swelling and ischemic necrosis of the wall of an internal carotid artery. It is considered that the common denominator in all 4 cases was the application of force to the carotid artery resulting in spasm of this vessel. Within 10 minutes there resulted dysfunction of the cerebral hemisphere on the same side which persisted for a period of time varying with the degree of anoxemia produced. There was swelling of the brain which probably reached its maximum in 24 hours and lasted at least three days. This brain swelling may be due, in part, to a vasoparalysis of the central nervous system which, in turn, may be closely associated with narrowing of the cerebral arteries. Furthermore, dilatation of the cerebral ventricles, especially that on the same side, may be a permanent residuum.

CONCLUSION

A syndrome of spasm of the internal carotid artery is described and consists of:

1. Dysfunction of a cerebral hemisphere.
2. Brain swelling, in the acute stage.
3. Internal hydrocephalus, in a late stage.
4. Narrowing of the cerebral arteries.

Cases are presented that illustrate the association of this syndrome with not only penetrating wounds of the neck but also blunt injuries of the head.

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NEUROGENIC OSSIFYING FIBROMYOPATHIES: A PRELIMINARY REPORT

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With the high incidence of injuries to the central and peripheral nervous system sustained in this war, a volume of neurosurgical material has become available for study. Late effects of spinal cord and peripheral nerve damage are still not thoroughly understood and it is obvious that treatment of patients with lesions of this type cannot be delayed until such additional knowledge is acquired. It therefore seems justifiable to record any observations made that may shed a certain amount of light on this only partially explored field. With this purpose in mind and without attempting to draw definite conclusions from the incomplete studies made, the results of a screening type of roentgen survey of a group of 62 male patients with lesions of the spinal cord and cauda equina are presented.

The particular feature of interest in the survey was the finding of soft tissue ossifications about the hips and in the lower extremities in 23 patients, only 3 of whom showed any clinical evidence of improvement.

Roentgen studies consisted of "scout" radiography of the lower extremities in the anteroposterior projection. Additional roentgenographic studies—stereoscopic anteroposterior, lateral and oblique projections—were made of the affected parts of some of the patients; "scout" examinations were performed of the upper extremities of several patients who presented abnormal findings in the lower extremities.

In each case, information was recorded regarding the date and character of the injury, the extent and location of lesions present, the date and nature of operative procedures, and the important clinical findings upon examination at this hospital. Blood calcium, phosphorus, phosphatase and total protein determinations were made of 27 patients. The appended chart records some of the more important features of the cases.

ANALYSIS OF MATERIAL

All patients gave a history of paraplegia affecting the lower extremities. Sixty-one of the 62 had sustained trauma of the spinal cord or cauda equina; one patient (Case 36) had non-traumatic spinal cord disease of unknown nature.

Of the 61 cases of traumatic origin, there had been immediate complete loss of motor and sensory function distal to the involved areas in all but 4. At the time of examination, these 4 patients (Cases 1, 2, 3, 4) showed clinical

* The author is indebted to Major Robert L. Craig, Major Helmuth Sprinz and other members of the staff of this Army General Hospital for assistance in performing the survey.

be demonstrable in cases where death ensues promptly. The further demonstration of changes in cerebral arteries in head injury may await the more frequent use of cerebral arteriography. Wakeley and Orley[7] state:

> In mild cases of cerebral concussion or contusion arteriography reveals a contraction of the blood vessels. In grave cases and in the presence of cerebral tumefaction the blood vessels are flattened and fill incompletely owing to vascular paralysis and mechanical compression.

SUMMARY

There have been presented 4 cases of dysfunction of the brain which are considered to be due to relatively mild trauma of the internal carotid artery. The first three were cases of penetrating wounds of the neck without laceration or thrombosis of the artery or any evidence of direct head injury. The fourth case was a blunt head injury with a fracture of the skull and postmortem evidence of brain swelling and ischemic necrosis of the wall of an internal carotid artery. It is considered that the common denominator in all 4 cases was the application of force to the carotid artery resulting in spasm of this vessel. Within 10 minutes there resulted dysfunction of the cerebral hemisphere on the same side which persisted for a period of time varying with the degree of anoxemia produced. There was swelling of the brain which probably reached its maximum in 24 hours and lasted at least three days. This brain swelling may be due, in part, to a vasoparalysis of the central nervous system which, in turn, may be closely associated with narrowing of the cerebral arteries. Furthermore, dilatation of the cerebral ventricles, especially that on the same side, may be a permanent residuum.

CONCLUSION

A syndrome of spasm of the internal carotid artery is described and consists of:

1. Dysfunction of a cerebral hemisphere.
2. Brain swelling, in the acute stage.
3. Internal hydrocephalus, in a late stage.
4. Narrowing of the cerebral arteries.

Cases are presented that illustrate the association of this syndrome with not only penetrating wounds of the neck but also blunt injuries of the head.

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NEUROGENIC OSSIFYING FIBROMYOPATHIES: A PRELIMINARY REPORT

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With the high incidence of injuries to the central and peripheral nervous system sustained in this war, a volume of neurosurgical material has become available for study. Late effects of spinal cord and peripheral nerve damage are still not thoroughly understood and it is obvious that treatment of patients with lesions of this type cannot be delayed until such additional knowledge is acquired. It therefore seems justifiable to record any observations made that may shed a certain amount of light on this only partially explored field. With this purpose in mind and without attempting to draw definite conclusions from the incomplete studies made, the results of a screening type of roentgen survey of a group of 62 male patients with lesions of the spinal cord and cauda equina are presented.

The particular feature of interest in the survey was the finding of soft tissue ossifications about the hips and in the lower extremities in 23 patients, only 3 of whom showed any clinical evidence of improvement.

Roentgen studies consisted of "scout" radiography of the lower extremities in the anteroposterior projection. Additional roentgenographic studies—stereoscopic anteroposterior, lateral and oblique projections—were made of the affected parts of some of the patients; "scout" examinations were performed of the upper extremities of several patients who presented abnormal findings in the lower extremities.

In each case, information was recorded regarding the date and character of the injury, the extent and location of lesions present, the date and nature of operative procedures, and the important clinical findings upon examination at this hospital. Blood calcium, phosphorus, phosphatase and total protein determinations were made of 27 patients. The appended chart records some of the more important features of the cases.

ANALYSIS OF MATERIAL

All patients gave a history of paraplegia affecting the lower extremities. Sixty-one of the 62 had sustained trauma of the spinal cord or cauda equina; one patient (Case 36) had non-traumatic spinal cord disease of unknown nature.

Of the 61 cases of traumatic origin, there had been immediate complete loss of motor and sensory function distal to the involved areas in all but 4. At the time of examination, these 4 patients (Cases 1, 2, 3, 4) showed clinical

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signs of improvement and roentgen studies showed absence of osteoporosis and no evidence of abnormal ossifications.

In 23 additional cases (all traumatic) there were on admission to this hospital clinical signs of returning function. Of these patients 15 had lesions of the cauda equina. Only 3 of the improved patients showed ossifications in the soft tissues:

The *first* (Case 25) was a 33-year-old medical officer who had been struck in the back by a sniper's bullet while riding in a jeep in France. He had immediate paraplegia and sensory loss below the 6th thoracic dermatome. Four days later, laminectomies of the 6th and 7th dorsal vertebrae were performed and a spicule of bone which was compressing the cord was removed; the cord appeared to be intact and pulsated normally. Upon examination 55 days later, a spastic paraplegia was present; there was slight sensory return in both lower extremities and slight abductor function in the right thigh. Radiography revealed a small deposit of amorphous new bone in the soft tissues above the left greater trochanter and below the neck of the left femur. No other ossifications were present and the bones showed no evidence of osteoporosis.

The *second* (Case 26) was a 31-year-old soldier who had been wounded in action in France by a bullet which penetrated his right posterior thorax and dorsal spine, producing an immediate complete paraplegia with dermatome level at T-9. A broncho-pulmonary fistula was complicated by persistent pneumothorax and empyema. Several days after injury, laminectomies were performed and the bullet was removed. The cord appeared to be contused but not severed.

About 5 days after injury, sensation began to return in both legs, and 15 days after injury, there was beginning recovery of motor function.

On admission, 68 days after injury, a small amount of osseous material was noted about the left greater trochanter; 43 days later, ossification had become abundant and was noted lateral as well as superior to the greater trochanter.

At this time, slight function was noted in all muscle groups; hypoesthesia was present below the T-9 dermatome level. The muscles of the lower extremities were atrophied and spastic.

The *third* (Case 27) had sustained a compression fracture of the 1st lumbar vertebra in a jeep accident. There was immediate paraplegia involving the cauda equina. Laminectomies of T-12, L-1 and L-2 were performed 11 days later and the cauda was found to be intact but compressed.

During the next few weeks there was slight return of sensation and motor function in the right foot, but none elsewhere.

Roentgen examination 90 days after injury revealed left renal calculi and soft tissue ossifications medial to the left knee. Reexamination 27 days later showed no increase in ossification. No other ossifications were noted in the lower extremities.

Of the 27 improving patients 10 showed varying degrees of osteoporosis in the bones of the lower extremities. In the entire group of 62 the only patients who had marked osteoporosis were 2 of those showing improvement, both with lesions of the cauda equina, and one of the unimproved patients who had osteoporosis in the bones of each tarsus but no osteoporosis elsewhere.

Of the 35 unimproved patients, 20 showed the presence of soft tissue ossifications—3 about both hips and both distal femora; 2 about both hips and 1 distal femur; 6 about both hips alone; 3 about 1 hip alone; 4 about both distal femora alone; 2 in 1 distal thigh alone. Of the 23 improved and unimproved patients with ossifications, 11 showed no evidence of osteo-

porosis, 8 showed slight osteoporosis, and 4 showed slight osteoporosis near the hips and knees and moderate osteoporosis in the bones about the ankles and in the feet.

Of the patients with ossifications, 19 had lesions of the thoracic cord with dermatome levels ranging from T-3 to T-10; 1 had a lesion of the low cervical cord with sensory level at C-7; 3 had lesions of the cauda equina with motor and sensory loss below the L-1 dermatome.

The earliest appearance of ossification was noted in Case 41, which was surveyed 40 days after injury. This patient showed minimal osseous deposits near the left greater trochanter. Cases 34 and 32, who were surveyed 45 and 48 days after injury, respectively, had rather extensive osseous deposits about each hip. Case 32 showed an additional large mass of osseous material medial to the left knee joint.

Of the 15 unimproved cases without ossifications, 7 showed no evidence of osteoporosis and 8 showed varying degrees, more prominent in the distal tibiae and fibulae and tarsal bones. Of these patients 13 had lesions of the thoracic cord and 2 had cauda equina lesions.

In none of the cases surveyed were roentgen abnormalities evident in the upper extremities.

Nearly all of the unimproved patients and all of the patients with ossifications either had decubitus ulcers or had had them. There was no definite correlation evident, however, between the locations of the ulcers and the osseous deposits. Several patients with ossifications near the hips or knees had no ulcers in these regions; in those that did, the ulcers were not near the areas of ossification.

As far as blood studies were concerned, there were no significant differences as regards blood total protein and calcium levels between the patients with ossifications and those without. However, in the group with ossifications, the average blood phosphorus level was 4.7 mg. and the average phosphatase level was 6.2 mg., while in the group without ossifications, the average phosphorus level was 3.9 mg. and the average phosphatase level was 5.2 mg.

There was no evident correlation between the time intervals from dates of injuries to dates of laminectomies, early and delayed operations having been performed with nearly equal frequency in both groups.

Of the patients with ossifications, 13 had flaccid paraplegias, the remaining 10 being spastic.

Nearly all of the patients had had infections of the urinary tract and suprapubic cystostomies had been performed on most of them. Eighteen patients were surveyed for evidence of urinary calculi; 3 of these, all of whom had soft tissue ossifications in the lower extremities, had multiple renal calculi.

Most of the patients with well-developed ossifications showed some restriction of motion of the joints adjacent to the osseous deposits. Only one patient, however, showed apparent ankylosis of the hips and knees and it

was not certain whether this was due wholly to the osseous deposits about the joints.

ROENTGEN APPEARANCE OF THE OSSIFICATIONS

In the early stages, the soft tissue deposits had a more or less amorphous cloud-like appearance similar to that noted in developing ossification of a hematoma. Even in the earliest cases studied, however, there was a definite tendency toward linear and trabecular structure.

In all cases examined 3 months or more after injury, the deposits had characteristics of trabeculated, cancellous bone with slender, interlocking

FIG. 1. Extensive ossifications about both hips, 6 months after onset of paraplegia resulting from epidural abscess with compression of the thoracic cord.

strands enclosing small ovoid or lozenge-shaped spaces between them. While some of the masses were discrete and moderately dense, in other areas the bone was laid down in sheets or bands which appeared to be distributed along muscle or fascial planes.

About the hips, the deposits were extra-capsular and most extensive above and anterior to the femoral necks and greater trochanters, although scattered osseous masses appeared about all margins and surfaces of the hip-joint capsules. When well-developed, they partially ensheathed the hip, extending from the pelvis about 1 cm. peripheral to the outer margins of the acetabulum to the upper shaft of the femur, to which they were attached a short distance below the lesser trochanter (Figs. 1, 2, and 3).

About the knees (Figs. 4 and 5), they were most prominent in the region of the medial collateral ligament, where in several cases they resembled the ossifications of Pellegrini-Stieda disease. In most cases, however, they were more extensive with bands of osseous tissue extending upward over the arch of the medial condyle, where they appeared to be attached to the periosteum of the distal third of the shaft of the femur. Ossifications were less abundant lateral to the knee, but here also they assumed a pattern similar to those noted on the medial side.

FIG. 2. Case 32. Early ossifications about right hip 48 days after injury.

Some of the ossifications terminated abruptly at the level of the knee joint space. In other cases, they extended about 1 cm. beyond the joint space. No ossifications were observed anterior or posterior to the knee.

FIG. 3. Case 37. Well-developed osseous deposits about both hips 91 days after injury.

Several patients showed isolated small islands of bone deep in the soft tissues of the thigh:

One (Case 29) had sustained a fracture of the lateral malleolus of the left fibula at the time of the spinal injury. One hundred and sixteen days later, partial union had taken place but no abnormal osseous deposits had appeared near the ankle, although rather extensive ossifications were noted about the hips and knees (Fig. 5).

FIG. 4. Case 32. Early ossifications about left knee 48 days after injury.

A second (Case 38) was found to have a dislocated right hip with chip fractures of the acetabulum and a chip fracture of the right patella. While osseous deposits were noted about both hips, they were less abundant about the dislocated hip than about the opposite hip and no deposits were noted about the knees. Normal callus was appearing about the chip fractures.

Another (Case 30) had a shell fragment in the right lateral knee joint space, partially embedded in the lateral tibial condyle. While a few osseous deposits were present medial and lateral to both knee joints, they were less abundant about the injured lateral condyle than about the corresponding portion of the other knee. The same patient, who also had moderately extensive osseous deposits about both hips, had several small metallic foreign bodies in the soft tissues of the right thigh and leg but no ossifications were noted about them.

One other (Case 45) had a small fragment of shrapnel in the soft tissues of the mid-thigh with no evidence of ossification about or near it.

CLASSIFICATION OF BONE, JOINT AND SOFT TISSUE LESIONS OF NEUROGENIC TYPE

Three principal types of lesions have been noted in the affected extremities following disease or injury of the spinal cord, dorsal nerve roots or peripheral nerves:

1. Osseous and muscular atrophy occasionally accompanied by retardation in bone growth from loss of motor innervation, as in acute anterior poliomyelitis and following severance of a nerve with motor components.

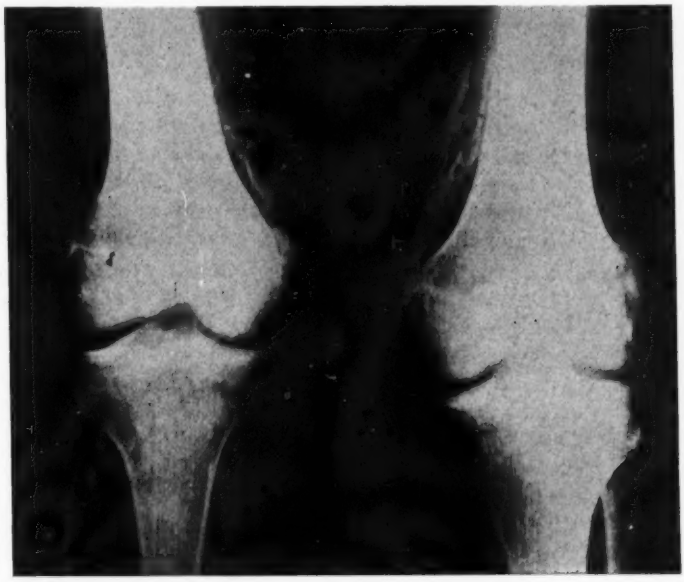

FIG. 5. Case 29. Both knees 116 days after injury.

2. Osteoarthropathies of the Charcot type from disease or injury of the afferent pathways of the cord, the dorsal spinal nerve roots or peripheral nerves.

3. Ossifying fibromyopathies without significant skeletal abnormalities, following trauma or disease of the spinal cord, cauda equina or peripheral nerves.

OSSEOUS AND MUSCULAR ATROPHY

The atrophy of muscle and bone resulting from motor paralysis is a well-known phenomenon.[11,14] The muscle atrophy usually affects certain selected groups; the bones show progressive deossification and occasionally impaired development or resorption with consequent diminution in size. Fractures may result from minimal trauma and, in the late stages, articular changes

similar to those seen in hypertrophic arthritis may appear in joints of the involved extremities.

During the first World War, Fleischhauer[6], Riedel,[13] Lehmann[10] and Maliwa[12] reported cases of atrophy following projectile wounds involving peripheral nerves. Atrophy may be confined to the juxta-articular portions of the bones or diffuse throughout them. Since bone atrophy is not a constant finding following lesions of this type and since it seems to be much less prominent in patients who are receiving passive motion and other types of physiotherapy, there is some evidence that it may be the result of disuse and impaired circulation.

OSTEOARTHROPATHIES OF THE CHARCOT TYPE

The conditions that have been reported as having produced Charcot joints are tabes dorsalis, syringomyelia, trauma to the spinal cord, cauda equina, dorsal nerve roots and peripheral nerves, congenital malformations of the spine (such as spina bifida), myelitis, lead poisoning, hemiplegia following cerebral hemorrhage, pressure on the cord or cauda equina from tumors or tuberculosis of the spine, progressive muscular atrophy (both the Aran-Duchenne type or chronic poliomyelitis and the spastic type or amyotrophic lateral sclerosis), typhoid fever, leprosy and peripheral neuritis.[1,2,4,11,16,17,18,19]

Similar lesions have been produced experimentally by Eloesser[5] and Corbin and Hinsey.[3] The latter deafferented and sympathectomized the hind limbs of cats by section of the L-4 to S-3 nerve roots and unilateral sympathectomy. No changes were noted in animals whose movements were restricted following operation. In similarly treated animals who were allowed to run free, a number developed changes resembling Charcot joints.

Several cases of osteoarthropathy have been reported as complications of injury of peripheral nerves. One of the most significant is the case described by Shands[17] in which a typical osteoarthropathy of the ankle followed traumatic severance of the posterior tibial nerve. During a two-year period after the patient sustained a crushing soft tissue wound of the leg without fractures, there gradually developed complete disintegration of the ankle and proximal tarsus with appearance of bony debris in the soft tissues about the joint. Duncan[4] described a somewhat similar case in a man who sustained traumatic severance of the dorsal roots of the lower cervical and upper thoracic nerves with subsequent development of an osteoarthropathy of the wrist.

While the mechanism of development of a Charcot joint is not entirely clear, the most widely accepted theory is that it results from trauma of an unprotected joint. With loss of afferent proprioceptive and pain impulses and retention of motor function, the patients continue to use the affected limbs but fail to protect them against the stresses and strains of everyday life.

The process usually starts with painless or nearly painless articular and

peri-articular soft tissue swelling which is followed weeks or months later by erosions and fragmentation of the bones about the joint. The fractured fragments rarely unite but increase in size by forming new bone about them. Frequently, long spicules of bone project for some distance into the surrounding soft tissues, and occasionally additional ossifications appear along the shafts of bones or in fascial planes some distance from the affected joint.

OSSIFYING FIBROMYOPATHIES

As noted by the author in a previous publication,[18] there have been a number of case reports in the literature of soft tissue ossifications without accompanying osteoarthropathy appearing as sequelae of injury or disease of the spinal cord or peripheral nerves. In 1921, Israel[7] described a case of traumatic severance of the cord which was followed by marked bone formation about one hip and both knees with long spurs of bone extending down the leg adjacent to the tibia. He also described a case with ossification about one hip joint following a gunshot wound of the spine with severance of the cord, two cases of paraplegia with ossifications about the knee joint capsule and in the vastus femoris muscle, and a case of myelitis in which a shell of bone surrounded the sciatic nerve. None of these patients showed fractures or other changes similar to those noted in tabetic osteoarthropathies.

Israel states that in 1868 Charcot described several cases of stab wounds of the spine that were followed by joint lesions of this type. He also mentions several other cases of a similar nature which were reported in the German and French medical literature.

Läsker[8] presented a case of alcoholic polyneuritis in which ankylosis of both hips was produced by calcification of the joint capsules and in which a lesser degree of calcification was present about the capsules of both knees.

Läsker, who believed that this was a form of myositis ossificans, quotes Oppenheim as having observed similar changes in alcoholic polyneuritis and Meyer as having reported ossification of the quadriceps muscles following a compression fracture of the spine with injury of the spinal cord.

Laux[9] reported a case of ascending paralysis with calcification of the soft tissues about one hip and in the muscles of the lower femur which appeared six months following the onset of the paralysis.

Schinz, Baensch and Friedl[15] state that parosteal new bone formation is not infrequently observed following injury or disease of the spinal cord, with deposits in tendons, muscles, joint capsules and periosteum of the paralyzed limbs, the trunk remaining free of ossifications. They quote Ceillier as having stated that up to 50 per cent of cases of myelitis develop ossifications. They report a case of tuberculosis of the spine with compression of the cord and consequent paraplegia and development of extensive ossifications about the hips and knees.

Brailsford[1] described a case in which a patient received a blow on the back of the neck which was followed by an immediate but temporary flaccid quadriplegia without sensory loss. Within two months there was soft tissue

TABLE 1. *Summary of data on 62 patients with paraplegia*

No.	Age	Immediate Motor and Sensory Loss	Dermatome Level on Admission	Type of Paraplegia on Admission	Blood Studies on Admission				Days after Injury to Roentgen Exam.	Clinical Improvement	Bone Atrophy	Soft Tissue Ossifications
					Total Protein	Calcium	Phosphorus	Phosphatase				
1	28	Partial	C-7 motor T-2 sens.	Flaccid					68	+	0	0
2	23	"	T-4 right 0 left	Spastic					82	+	0	0
3	—	"	L-1 to S-5	Flaccid					145	+	0	0
4	24	"	T-10	"	7.6	10.6	4.4	7.8	67	Slight	0	0
5	23	Complete	L-1 to S-5	"					78	"	0	0
6	18	"	L-1 to S-5	"					145	+	Marked	0
7	19	"	S-4, 5	"					78	+	0	0
8	30	Complete	L-5 to S-5	"					375	Slight	Marked	0
9	31	Complete	L-1 to S-5	—	8.5, 6.2	10.4	4.4	4.0	63	+	Slight	0
10	25	"	L-1 to S-5	Flaccid	5.8, 6.8	9.3	4.2	4.2	101	+	"	0
11	24	"	L-1 to S-5	"	7.0, 7.2	12.0	3.8, 3.7	2.7	68	+	"	0
12	31	"	L-1 to S-5	"	7.4, 6.9	12.0	3.6	5.2	48	+	0	0
13	38	"	L-1 to S-5	"	6.5, 7.5	—	4.4	8.6	137	+	0	0
14	20	"	C-7 motor T-3 sens.	Spastic					111	Slight	0	0
15	30	"	T-6	"					131	+	Slight	0
16	28	"	T-4	Flaccid					187	Slight	Moderate	0
17	26	"	T-10	Spastic					97	+	Slight	0
18	24	"	T-8	"	7.5, 7.4	11.4	3.8	4.8	88	+	0	0
19	—	"	T-9	"					236	+	0	0
20	20	"	L-1 to S-5	Flaccid	7.9	12.0	4.0	7.2	60	+	0	0
21	24	"	L-1 to S-4	"	6.1				98	+	0	0
22	21	"	L-1 to S-4	"	6.2				122	+	0	0
23	24	"	L-1 to S-5	"	8.4	9.2	3.0	2.2	103	+	0	0
24	23	"	L-1 to S-5	"	7.6	9.8	4.5	10.0	18	+	0	0
25	33	"	T-6	Spastic	7.7, 8.6	10.5	4.4	6.8	55	+	0	Left hip
26	31	"	T-9	"	6.9	10.4	6.1	5.4	68	+	Slight	Left hip
27	24	"	L-1 to S-5	Flaccid	7.0, 7.8	11.7	4.8	4.0	90	Slt.-rt. 0-lt.	"	Left knee
28	28	"	C-7	Spastic					105	0	0	Both hips & knees Left mid-thigh

28	28	"	C-7	Spastic					165	0		Left mid-thigh
29	24	"	T-6	"	6.8, 6.9	9.6	4.0	6.8	116	0	Slight	Both hips & knees
30	30	"	T-9	Flaccid	7.9, 6.8	13.8	6.0	6.3, 4.8	111	0	Moderate	Both hips & knees
					6.9							
31	24	"	L-1 to S-5	"	6.8, 7.5	12.6	4.8	5.5	119	0	Slight	Both hips & left knee
32	20	"	T-4	"	7.1, 7.5	9.0	3.1	7.2	48	0	0	Both hips & left knee
33	—	"	T-5	Spastic					116	0	0	Both hips
34	33	"	T-3	Flaccid					45	0	0	Both hips
35	22	"	T-4	Spastic					76	0	0	Both hips
36	28	"	T-5 to T-7	Flaccid					180	0	Moderate	Both hips
37	24	"	T-9	"	6.5, 7.2	9.9	5.0	5.2	91	0	Slight	Both hips
					5.4							
38	33	"	T-4	Spastic	8.0, 7.2	9.8	5.3	4.3	183	0	"	Both hips
39	19	"	T-7	"					87	0	"	Left hip
40	25	"	T-10	Flaccid	6.2	9.4	5.0	4.8	59	0	0	Right hip
41	26	"	T-8	"	6.6, 5.5	9.2	4.3	3.4	40	0	0	Left hip
42	24	"	T-5	"	7.6	11.0	6.4	9.7	74	0	0	Lower thighs
43	28	"	T-6	"	6.7	9.0, 12.6	4.0, 3.4	5.1, 13.0	91	0	0	Both knees
44	20	"	T-3	Spastic					320	0	Moderate	Both knees
45	24	"	T-5	Flaccid					127	0	Slight	Both knees
46	24	"	T-3	Spastic					91	0	0	Left knee
47	29	"	L-1 to S-5	Flaccid					160	0	Moderate	Left lower thigh
48	28	"	T-3	"					125	0	Slight	0
49	28	"	T-7	Spastic					130	0	"	0
50	19	"	T-10	Flaccid					103	0	Moderate	0
51	—	"	T-1	"					110	0	Slight	0
52	24	"	L-5 to S-5	"					128	0	Moderate	0
53	24	"	T-11	"					347	0	0-Hips Marked-Ankles	0
54	35	"	T-11, 12	"					123	0	Slight	0
55	23	"	T-4	"	7.4		4.2	5.3	44	0	0	0
56	28	"	T-9, 10	"					77	0	Slight	0
57	20	"	T-7	"					123	0	0	0
58	25	"	T-3	"					75	0	0	0
59	30	"	T-7	Spastic	6.8, 5.8,	10.8	5.2	3.0	91	0	0	0
					7.5, 7.5							
60	31	"	T-7	"	6.9, 8.2	10.0	4.0	4.4	61	0	0	0
61	25	"	T-3	"					132	0	0	0
62	22	"	L-1 to S-5	Flaccid	6.5,7.0	10.8	3.1, 3.3	3.0	73	0	0	0

swelling about both elbows with appearance of flocculent deposits of calcium around the joints; within a year, the joints were surrounded by masses of ectopic bone. No abnormalities were noted in the bones. It was believed that the patient had sustained a hemorrhage into the cord (hematomyelia).

A few years ago, the author observed a case of epidural abscess which was followed within six months by the appearance of extensive ossifications about both hips:

The patient, a girl 20 years of age, was admitted to the Mary Fletcher Hospital, Burlington, Vermont, on November 8, 1939, with complete paraplegia below the 10th thoracic dermatome of 24 hours' duration. About two weeks before, the patient had had a furuncle on the face which was squeezed. About one week prior to admission, she noted pain in the back and abdomen and elevated temperature.

On admission to the hospital, a diagnosis of epidural abscess was made and exploration on the same day revealed an abscess which was drained and which ultimately healed. There was no return of cord function, however, and the patient had a spastic paraplegia with complete sensory loss. Intermittent urinary tract infection was controlled by tidal drainage until the patient developed an automatic bladder.

Roentgen examination of the spine, pelvis and hips had revealed no abnormality on admission. About six months later, an excretory urographic study was made, at which time ossifications were noted about both hips (Fig. 1). On the right side, a large buttress of coarsely trabeculated bone extended outward from the pelvis above the acetabulum to surround the greater trochanter. The left hip joint and upper extremity of the femur down to a point 5 cm. distal to the lesser trochanter were completely encased in bone. No ossifications were discovered in the more distal portions of the lower extremities, and no atrophy, erosions or fractures were noted in the bones.

NATURE OF THE OSSIFICATIONS

An adequate explanation for the appearance of the soft tissue ossifications cannot be offered on the basis of evidence collected to date. While there is a slight resemblance between the ectopic bone deposits noted in clinical and experimental Charcot joints and the ossifications of paraplegia, in the former they rarely appear until after the bones fracture, while in the latter they are not associated with fractures or other significant abnormalities of bones and joints.

In comparing these patients with the group of unaffected patients who sustained similar lesions of the cord and cauda equina, there appeared to be no significant differences with regard to severity of injuries, sites of neurologic lesions, time of operative treatment, presence or absence of decubitus ulcers, urinary tract infection or associated injuries or infections, ages of patients, or blood calcium and total protein levels.

One finding which may be of prognostic significance is the fact that of the group with ossifications, only 3 out of 23 showed any clinical evidence of improvement, and in 1 of the 3 there was no improvement in the extremity showing ossification. The absence of osteoporosis in a large number of these patients and the relatively high blood phosphorus and phosphatase levels in this group may also be of some importance. The incidence of renal calculi was slightly high, but this again is of doubtful significance.

Since the lesions resemble in certain respects the changes noted in ossifying hematomas, it may be argued that they follow unrecognized

trauma to the soft tissues with hemorrhage and subsequent ossification. It is curious, however, that the patients who sustained definite trauma to the hip, knee and ankle showed no osseous deposits of consequence in these areas.

SUMMARY

A group of 62 patients with paraplegia due to injury or disease of the spinal cord and cauda equina were surveyed radiographically. Twenty-three of these patients, all but 3 of whom showed no clinical evidence of improvement, were found to have ectopic deposits of osseous material in the soft tissues of the affected extremities, chiefly in the vicinity of the hips and knees.

Attention is called to this condition as an apparently common complication of injury or disease of the spinal cord and cauda equina.

The condition is differentiated from the atrophic type of lesion noted with impairment of motor nerve function and the osteoarthropathic type of lesion with impairment of afferent nerve function.

Due to the preliminary nature of the study, no conclusions of consequence are drawn. However, several avenues for future investigation are suggested from the findings listed.

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SEROUS MENINGITIS*

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NEUROLOGISTS and neurosurgeons have long been troubled by a heterogeneous group of patients who showed evidence of increased intracranial pressure but who proved not to have space-occupying lesions. Some of these patients have a history of an infection contiguous to the intracranial cavity in ears, mastoids, or sinuses. They are suspected of having a brain abscess. A few have had an injury to the head and are thought to have subdural hematomas. Others have no history of infection or injury and are considered to have brain tumors.

These cases have been variously referred to as "pseudo-tumors," serous arachnoiditis, serous meningitis, chronic arachnoiditis, toxic hydrocephalus, otitic hydrocephalus, meningitis sympathica, aseptic meningitis and so on. The wide variety of terminology clearly indicates the general confusion regarding them.

Quincke[10] reported ten cases of serous meningitis and emphasized the spinal fluid findings and the increase of intracranial pressure. Passot,[9] in a thesis, distinguished between the purulent and non-purulent complications of otitis media. He differentiated them by spinal fluid examination. The non-purulent group was considered due to an excess of cerebrospinal fluid in the subarachnoid spaces. Warrington[13] in 1914 described five groups of intracranial serous effusions of inflammatory origin: those due to otitis media, to tuberculosis, to specific fever, to head injury, and finally an unexplained group. As his title indicates, he considered a near or distant focus of infection as the primary origin. Claude[2] discussed the subject thoroughly. He gave trauma, infection, and encephalitis as the etiologic factors and emphasized the value of air studies in differential diagnosis.

More recently Symonds,[12] Davidoff and Dyke,[3] McAlpine,[8] Howell,[6] and Sahs and Hyndman[11] have contributed to this subject. The majority of authors have advocated conservative treatment, once the condition was recognized, with repeated spinal drainages and dehydration of the patient. Davidoff and Dyke,[3] in contrast, advocated subtemporal decompression as a routine measure. The need for air studies to differentiate space-expanding lesions is admitted by most authors, although Symonds[12] did not use them in his three cases and McAlpine[8] in only two of his five cases.

It is obvious from a review of the literature that these patients all recovered spontaneously or at least with conservative treatment. However, in many instances it is not clear as to whether impairment of vision occurred in the patients who were treated expectantly or conservatively. McAlpine[8]

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reports optic atrophy in one of his cases and it is to be suspected that this complication may have occurred more often than had been reported.

CASE REPORTS

Case 1. An early experience with a case of "pseudo-tumor" was that of Mrs. J. H. G., a 49-year-old woman, first seen in February 1935. At that time she complained of failing vision, nausea and vomiting, and dizziness during the preceding year with tinnitus for one month. The past history was not relevant except for periodic frontal headaches occurring on an average of once monthly since the age of 18. There had been no change in the intensity and frequency of these headaches during the preceding year. General physical and neurological examinations revealed no significant findings except bilateral papilledema of 3 to 4 diopters with reduction of vision to 0.2 in each eye.

Under the assumption that we were dealing with an unlocalized brain tumor, ventriculography was performed. Both ventricles were tapped and each contained about 15 cc. of fluid. X-rays taken after replacement of the fluid by air failed to disclose any abnormalities of the ventricular system. A few days later formal right subtemporal decompression was carried out. The brain appeared normal but the leptomeninges were thought to be somewhat thickened and opaque, and there was an unusual amount of subarachnoid fluid.

Convalescence was uneventful and the patient left the hospital on the 17th postoperative day. She lives in another city and has not been seen since three months after the operation. At that time the margins of the optic discs were blurred but there was no elevation. Vision was 1.0 in the right eye and 0.8 in the left. The decompression bulged moderately. We have heard from her at intervals since; the last report was in August 1944. Her vision had not changed. There was still slight bulging of the decompression, indicating the persistence of a mild degree of increased intracranial pressure.

Comment. It does not seem likely that this woman's vision would have been spared without decompression. No etiologic factors for her intracranial condition were ever discovered.

Case 2. A similar case, but with chronic infection present elsewhere in the body as a possible etiologic factor, was that of F. H., an 11-year-old boy seen on the children's orthopedic service at the Cook County Hospital in March 1935. He had been under treatment for chronic osteomyelitis of the left femur and humerus of 2 years' duration. Headaches had been present for 3 weeks, and 2 weeks before he had developed diplopia and begun to vomit frequently. Examination revealed slight weakness of the right side of the face, bilateral abducens palsy, and bilateral papilledema of 2 to 3 diopters. X-rays of the chest were negative.

He was thought to have a metastatic brain abscess, and ventriculography was performed. The ventricles appeared to communicate at the time of the air injection but the roentgenograms showed poor filling of the left ventricle with no air in the third. A left subtemporal exploration and decompression were carried out. There was more than the usual amount of subarachnoid fluid but the brain itself appeared normal without any evidence of an intracranial lesion. When a cannula was introduced into the temporal lobe, the temporal horn of the ventricle was readily entered and about 30 cc. of clear fluid were aspirated.

The child made an uneventful convalescence and the papilledema and abducens palsy rapidly receded. Bulging of the decompression was marked for the first month; the bulging could be collapsed temporarily by spinal drainage. Gradually the decompression ceased to bulge and by dismissal 2 months after operation it was flat.

Comment. This patient might well have been treated by conservative means. However, the ventriculograms misled us as they appeared to substantiate the clinical impression of a left temporal lobe abscess. Accordingly surgery was performed without any further delay.

Case 3. A very striking case was that of Mrs. G. R., a 24-year-old white woman, first seen in October 1937. She had been admitted to the hospital one month before because of headaches and pain over the left mastoid of 2 months' duration. Bilateral otitis media had been present since childhood and a right mastoidectomy had been performed a year before. The patient had recurrent chills, with her temperature rising to 103 at times. She complained of severe headache and vomited frequently. After treatment with sulfonamides for a few days her condition improved and a left mastoidectomy was performed. Two days later the chills recurred and her fever rose to 104. On the 4th day after the mastoidectomy the left lateral sinus was explored. Free bleeding occurred from the upper end but not the lower, so that the internal jugular vein was ligated in the neck. Following this procedure the temperature fell to normal and the patient's general condition improved. However, drowsiness and at times stupor appeared; she complained again of severe headache and vomited frequently. Three weeks after the operation on the lateral sinus the patient was found to have bilateral papilledema of 2 to 3 diopters, and neurosurgical consultation was called.

Neurological examination revealed slight weakness and incoordination of the right extremities and slight weakness of the left lateral rectus muscle. The spinal fluid pressure was 320 mm.; the fluid was clear, and contained only 3 cells. The case was not thought to be one of abscess and treatment was conservative for 2 weeks. During that time several spinal punctures were made with removal of 20–30 cc. at each tap. The pressures ranged from 150–500 mm. of water. At the end of that time the papilledema was observed to be increasing with several fresh retinal hemorrhages. There was no progression in the neurological findings and perimetric fields were normal for both form and color.

Ventriculography was attempted. Both lateral ventricles were tapped, but only a few cc. of fluid were obtained from each and air injected escaped immediately from the cannulae; X-rays failed to show any air in the intracranial cavity. Following this the patient had severe headache, was restless, and claimed that she could not see. She was given 250 cc. of 25 per cent sucrose intravenously. The next day her general condition was good. The pupils reacted to light but the patient denied light perception. The spinal fluid pressure was 450 mm. of water.

Left subtemporal exploration and decompression were carried out the following day. The brain was under marked tension when the dura was opened but there was no widening of the convolutions. The brain was injected and there was a grey-yellow exudate along the larger cortical vessels. Exploration of the temporal lobe with a cannula yielded no evidence of an abscess.

Convalescence was uneventful from a general standpoint. The patient was confused and irrational for several days. Spinal punctures continued to show fluid under pressure of 300-400 mm. Cultures were repeatedly negative. At dismissal on the 12th postoperative day the patient was normal mentally, the decompression bulged moderately, the fundi showed 2–3 diopters of elevation bilaterally but all hemorrhages and exudates were absorbed, and the patient could read newspaper print.

Her later course has been of the greatest interest. The papilledema slowly receded and disappeared within 6 weeks after dismissal. At no time has it recurred. Vision was 0.8 in each eye 6 weeks after dismissal and has remained at that level. Moderate to marked bulging of the decompression was present during the first year and the patient complained of persistent headaches. Drainage persisted from both ears. At the end of that time a radical mastoidectomy was done on the right side. Since then she has had very little drainage from the right ear and much less headache and bulging of the decompression.

Two years after her decompression she had an uneventful pregnancy and delivered a normal child. The pregnancy had no effect on the bulging of the decompression. Three years later she had another child. Gradually the decompression has ceased to bulge significantly, although it is never completely flat. She occasionally has a recurrence of drainage from both ears, often as a result of an upper respiratory infection. At such times headaches recur and the decompression bulges markedly. When last seen in December 1944, over 7 years after her de-

compression, there was still very slight bulging of the decompression. She had no complaints, vision was 0.8 in each eye and the fundi were normal.

Comment. The prolonged increase of intracranial pressure and the clear relationship of its exacerbations to the exacerbations of the chronic otitis is very striking. It is very doubtful if this patient's vision could have been preserved without decompression.

Case 4. Another case of clear otitic origin was that of R. C., an 8-year-old girl seen on the otologic service at the Cook County Hospital in April 1938. Three months before she had had right mastoiditis and lateral sinus thrombosis for which mastoidectomy and ligation of the internal jugular vein had been performed. Bilateral papilledema had been noted since that time.

Neurological examination was negative except for bilateral papilledema of 2 to 3 diopters and enlarged blind spots in the perimetric fields. Vision was 1.0 in each eye.

Ventriculography was performed and communication of the lateral ventricles was demonstrated. The roentgenograms showed poor filling of the right lateral ventricle, and a right subtemporal exploration and decompression were performed. The cortex of the temporal lobe was injected and the brain was under increased pressure. However, exploration of the temporal lobe with the brain cannula showed no evidence of abscess.

The child's convalescence was complicated by epidemic parotitis but she left the hospital on the 23rd postoperative day. She was seen at intervals after this and within 3 months the fundi were normal. The decompression continued to bulge for 3 or 4 years. When the child was last seen in 1943, over 5 years after operation, she was perfectly well, the operative site was depressed and she requested repair of the skull defect. After the lack of necessity for that was explained to her she was satisfied.

Comment. Localization of this type of lesion to the posterior fossa produces an internal hydrocephalus with a clinical and ventriculographic picture that suggests posterior fossa tumor. Horrax[5] differentiated between chronic serous arachnoiditis of a generalized character and chronic circumscribed or cystic arachnoiditis, a localized process which he considered the sequel of a meningoencephalitis. He reported 33 cases of generalized chronic serous arachnoiditis of the posterior cistern which he divided into acute or subacute, chronic and otitic cases.

Case 5. The first experience with arachnoiditis of the posterior fossa was the case of E. F., a 14-year-old girl first seen in November 1935 at the Cook County Hospital. Two years before she had complained of stiff neck and headache and, under a diagnosis of cervical Pott's disease, was kept in bed for 8 months. She was then well until a month before, when there was sudden onset of headache and great irritability and restlessness. She had improved after two spinal drainages.

Examination showed a frail blonde child who appeared to be only about 10 years of age with no development of secondary sex characteristics. She was unable to stand or walk without support and there was marked hypotonicity of all the skeletal muscles. There was a bilateral Hoffmann sign and the Chaddock, Gordon and Oppenheim signs were present bilaterally. No Babinski could be obtained but there were a few jerks of ankle clonus on the left. There was bilateral pallor of the optic disc with moderate loss of substance. Vision was reduced to 0.01 in the right eye and 0.1 in the left. The child was talkative, euphoric and facetious with frequent changes of mood. She was apparently somewhat precocious but had little insight.

The spinal fluid was slightly xanthochromic and under marked pressure. It contained no cells, and a guinea pig inoculated with it failed to develop tuberculosis. X-rays of the skull

showed marked pressure digitations, separation of the sutures, and erosion of the posterior clinoid processes.

She was thought to have a brain tumor but the localization was not clear. Ventriculography demonstrated a marked symmetrical internal hydrocephalus. This was thought to indicate a posterior fossa tumor and a suboccipital craniectomy was carried out. There was no evidence of tumor in the posterior fossa but the arachnoid over the posterior cistern was thickened and opaque. When it was opened the fourth ventricle was seen to be considerably dilated. The arachnoid of the posterior cistern was widely resected and the wound was then closed.

Convalescence was satisfactory. At dismissal she could walk but was moderately ataxic. The mental attitude was the same and the visual acuity had not improved.

She was seen 2 years later and presented at a clinic. The decompression was flat and there was no ataxia. Visual acuity was 0.1 in the right eye and 0.6 in the left. She seemed perfectly well at that time. However, a month later she returned to the hospital complaining of headache, blurred vision and stiff neck. The decompression bulged markedly but could be collapsed by spinal drainage, which gave the patient marked relief. The spinal fluid contained 8 lymphocytes.

An attempted encephalogram was unsuccessful. A ventriculogram showed marked internal hydrocephalus. The fourth ventricle was visualized and markedly distended. Re-exploration was carried out. Exposure of the posterior cistern and fourth ventricle was very difficult because of adhesions. The posterior cistern was obliterated except for several pockets of clear fluid. The child did not rally after operation and died the following day.

Comment. Horrax[5] reported a death in his series after operation for recurrence of symptoms.

Case 6. Another patient with posterior fossa arachnoiditis is still under observation with symptoms that suggest the process is present in other parts of the intracranial cavity. R. H., a 40-year-old woman, was first seen at Mercy Hospital in April 1941. She had had multiple operations in the past including an appendectomy, thyroidectomy, and cholecystectomy and had been under treatment for peptic ulcer and colitis for the preceding 3 years. A thrombophlebitis of the left lower extremity had followed the cholecystectomy.

Recurrent headache with associated vomiting had been present for 2 years. For the preceding 2 months there had been more severe and pronounced headache, and dizziness, even in the horizontal posture, had developed. Blurring of vision had been present for 1 month.

Neurologic examination was essentially negative except for slight increase of the tendon reflexes on the left with a few jerks of ankle clonus on that side. There was bilateral papilledema of 2 to 3 diopters which the ophthalmologist felt had been present for some time. Vision was 0.8 in each eye and the perimetric fields were normal.

A ventriculogram revealed a symmetrical internal hydrocephalus. The patient was thought to have a posterior fossa tumor and a suboccipital craniectomy was performed. When the dura was opened there was a large arachnoid cyst situated in the midline over the posterior cistern and separating the lower part of the cerebellar hemispheres. The cyst measured approximately $3 \times 3 \times 5$ cm. and contained clear fluid. After its evacuation, thorough exploration of the posterior fossa failed to reveal any neoplasm and the wound was closed. The dura, perhaps unwisely, was sutured.

Microscopic examination of the wall of the cyst revealed moderate thickening of the arachnoid with occasional small plaques of cellular proliferation and a rare cystic space. The pathologic diagnosis was chronic, non-specific arachnoiditis with inclusion cysts.

The patient's convalescence was prolonged. Headaches, vomiting, and dizziness persisted. Spinal drainages on numerous occasions revealed manometric pressures ranging from 190 to 400 mm. of water. The total protein was 100–120 mg. and there was a persistent pleocytosis of 140–416 cells which were all lymphocytes. Repeated cultures failed to show any bacterial growth. She was finally dismissed on the 40th postoperative day.

She has been seen at frequent intervals. There has never been any bulging of the suboccipital decompression. The papilledema slowly receded but slight elevation of the discs has persisted and is still present. The spinal fluid pleocytosis finally disappeared. After 8 months the patient returned to her work as a secretary, but frequent headaches and vomiting have persisted. These are temporarily relieved by spinal drainages or intravenous injections of hypertonic sucrose solution. The spinal manometric pressure is always increased and is usually 300–400 mm. of water. An encephalogram in June 1943 revealed the symmetrical internal hydrocephalus to be present still, with the ventricles a little larger than 2 years before.

Her vision remained at 0.8 in both eyes until recently, and no defects of the visual fields were noted. However, her ophthalmologist has recently found her vision to be reduced to 0.5 O.U. and the perimetric fields now show a partial upper quadrant homonymous defect.

Comment. It is now felt that this patient's arachnoid cyst with consequent obstructive hydrocephalus was only part of the process of generalized chronic serous arachnoiditis. It would appear that she may suffer from another phase of that condition, opticochiasmal arachnoiditis, which Lillie[7] has described. In retrospect it was a mistake to close the dura at the time of the operation. If the dura had been left open, persistent bulging of the suboccipital decompression would probably have occurred and the patient's course might have been much better. A transfrontal exploration of the optic chiasm with generous subtemporal decompression seems indicated now that vision has begun to fail and field defects have appeared. However, we have been reluctant to undertake further surgery on this woman.

DISCUSSION

These six cases illustrate some of the problems in a group of patients who can be briefly described as having subjective symptoms suggesting increased intracranial pressure and showing papilledema. Neurological findings, exclusive of those associated with increased intracranial pressure, are minimal and definite localization is seldom suggested. A near or distant focus of infection may be present. If so, abscess is correspondingly suspected; if not, neoplasm is the favored diagnosis. The cerebrospinal fluid manometric pressure is high; the fluid is clear or contains only a few lymphocytes. Air studies fail to show any evidence of a space-occupying lesion unless the arachnoiditis involves the posterior cistern; in that case an internal hydrocephalus is demonstrated. In this last group the indication for operation is clear; unfortunately the results are not always satisfactory. Horrax[5] reported five deaths in 33 cases within two years after operation. Of the remaining 28 he classified 14 as improved and 14 as well. Barré[1] reported three cases of arachnoiditis of the posterior fossa that were operated on with one death.

Examples due to trauma have not been included in this paper. However, on the neurosurgical service at the Cook County Hospital patients are frequently seen who develop choked discs after head injury. Other signs of subdural hematoma are absent. Some of these patients have been explored with negative results; others have been treated conservatively with dehydration and spinal drainages and the papilledema has subsided and the subjective symptoms disappeared. It is difficult to say whether the pathology in these

cases is an inflammatory reaction in the leptomeninges secondary to trauma, or a late chronic cerebral edema, or whether there is some other explanation. It is my impression that these patients usually have suffered subarachnoid hemorrhage, but, on the other hand, many cases of traumatic or spontaneous subarachnoid hemorrhage fail to show any evidence of papilledema.

This whole subject is very troublesome and difficult for the neurosurgeon. The cases that I have presented represent only one group of the heterogeneous "pseudo-tumors," that with objective evidence of increased intracranial

TABLE I. *Classification of serous meningitis (intracranial)*

A. LOCATION

1. GENERALIZED—serous arachnoiditis
2. LOCALIZED
   a) Cerebral hemisphere—often associated with a localized encephalitis—meningoencephalitis
   b) Optic chiasm—opticochiasmal arachnoiditis
   c) Posterior cistern—cisternal arachnoiditis

B. ETIOLOGY

1. OTITIC—otitis media—mastoiditis—sinusitis
2. TRAUMATIC—(subarachnoid hemorrhage?)
3. TOXIC—focus of infection at some distant point
4. UNKNOWN

C. TYPE

1. ACUTE OR SUBACUTE—inflammatory
2. CHRONIC—fibrous or proliferative (hyperplastic)

pressure. An even more obscure and difficult type is the patient who has headache and often other subjective evidence of intracranial pathology, with perhaps some objective neurological findings, but who does not have objective evidence of increased intracranial pressure. Some of these patients have convulsive seizures which may be quite localized in nature. Air studies may be misleading, as in Cases 2 and 4. Exploration reveals no evidence of neoplasm or perhaps no gross pathology at all. In some cases there are localized thickening and opacity of the arachnoid, localized shrunken or atrophic areas of cortex or combinations of both.

Another type is the localized arachnoiditis of the optic chiasm. Here, as a rule, the symptoms and objective findings point to a lesion of the optic chiasm, or of the optic nerves anterior to the chiasm. Surgery may at times give dramatic improvement, or again the results may be equivocal or a failure.

A review of the author's experience discloses that over a period of ten years there have been 43 intracranial explorations in which no neoplasm or abscess was found and the diagnosis of serous meningitis or its equivalent was made (Table II). Some of these patients have not been followed and may later have shown definite evidence of cerebral tumor. However, a considerable group have been followed long enough to be reasonably certain that a space-occupying lesion does not exist. The majority of the patients have

shown symptomatic improvement after operation; at times this has been dramatic. On the other hand, in many cases it could be reasonably argued that they might have done equally well without operation. In some (Case 5) the patient was temporarily improved, with later return and even exacerbation of symptoms.

Most of the deaths occurred in the cases of posterior fossa involvement, as there were five fatalities in the nine cases of this group that were operated on.

In this series, as well as in most reported, there is an unfortunate lack of pathologic studies. This is partly explained by the difficulty of getting adequate biopsies at operation. The report of Davis and Haven[4] is in marked

TABLE II. *Classification of author's cases*

	Cases	Deaths
Generalized serous arachnoiditis	15	1
Localized		
Cerebral hemisphere (meningoencephalitis)	11	1
Opticochiasmal arachnoiditis	8	0
Posterior cisternal arachnoiditis	9	5
TOTAL	43	7 (16%)

contrast to most of the literature, as these authors studied the arachnoid membrane in ten cases of this type. They divided their cases into three groups: the first, inflammatory (1 case); the second, fibrous (7 cases); and the third, hyperplastic (2 cases). In the last group cellular infiltration of the arachnoid was so marked that the authors raised the question of a possible neoplasm. Both of these patients were still living and well at the time of the report.

Table I represents an attempt at classification of the various intracranial types of serous meningitis. It is not original but rather is a combination of various classifications advanced by several authors, especially Claude[2] Horrax,[5] Howell,[6] Warrington,[13] and Davis and Haven.[4] It does attempt to separate the various classifications which have been made into comparable headings.

The great need is for more adequate correlation of microscopic findings with clinical types of serous meningitis. The careful study of individual cases may seem unproductive and disappointing but if persisted in should eventually shed further light on this obscure syndrome.

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PREVENTION OF NERVE REGENERATION AND NEUROMA FORMATION BY CAPS OF SYNTHETIC RESIN*

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THE ACUTE PAIN that is associated clinically with the formation of neuromas following the section of peripheral nerves in amputations has led to the introduction of various procedures designed to suppress the regeneration of nerve fibers from the cut (for literature, see Guttmann and Medawar,[2] and Boldrey[1]). Surgical interventions have been aimed mainly at blocking or diverting fibers rather than suppressing their growth and have been only partially effective in preventing neuroma formation, while chemical and physical treatments, which eliminate living fibers from the nerve end, have yielded varying success depending on the agent used. From the experiments of Guttmann and Medawar[2] it has become apparent that to inhibit the formation of a neuroma, the old axons in the terminal segment of the nerve stump must be killed and this segment rendered impervious to regenerating fibers; mere blocking is insufficient.

In addition, experimental studies on the effects of prolonged denervation are frequently thwarted by the reconnection of nerve fibers that have escaped from inadequately blocked proximal stumps or have spanned extensive resection gaps. This is true particularly in the case of small nerves, which are technically difficult to handle, or in small animals, where regeneration distances are short. But even for larger experimental nerves, previously suggested methods are inconvenient when it comes to treating a number of animals.

In several series of experiments on rat nerves, a rapid, simple method has been developed which is effective both in impeding fiber regeneration and preventing neuroma formation. Approximately 75 nerves of white rats (100 to 300 gm.), including femoral, sciatic, facial and lumbar branches (0.2 to 1.5 mm. in diameter), were treated as follows:

The nerve was exposed for 5–10 mm. and transected. The distal end of its proximal stump was then coated for a distance of 3–4 mm. with a thin (10 per cent) solution of methylmethacrylate polymer in acetone. The plastic hardened rapidly, and defects in the cap produced by shrinkage were repaired with a second or third coating. When the surface of the final coat had hardened, the nerve was returned to its bed and the wound sutured.

Occasionally, the epineurium was pulled down over the cut surface and ligated before applying the plastic but the results were equally satisfactory without this procedure. The caps were left in place for a few days to one year.

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FIG. 1. Longitudinal section through the capped segment of a nerve showing the tapering which occurs in the enclosed portion. No swelling appears proximally and the regeneration of nerve fibers has been effectively prevented. *c*, cap; *s*, liquid-filled space. 1 year postoperative. Bodian impregnation, ×43.

When the nerves were reexposed, the caps were found to be firmly adherent to the nerve ends. Electrical stimulation tests proved that in all but one case no fibers had escaped either through or around the cap. Adhesions between the plastic and the surrounding tissues were minimal, and even after one year, no large swellings were present in the proximal portions of the nerves. In a few instances where the cap had contracted excessively, constricting the nerve end, the diameter of the nerve proximally was slightly larger than normal, but the typical bulbous enlargements associated with neuromas were not observed.

The histological features of the capped segment are illustrated in Fig. 1, showing the buccal branch of a facial nerve removed one year after operation. Proximally, the diameter of the nerve remains unchanged down to the level of the cap. Within the latter, the nerve tapers to a point; there is a space, apparently filled with serous fluid, between the nerve and the plastic which has prevented any adhesion between them and eliminated any possibility of pressure on the axons. A thin fibrous capsule, which is continuous with the epineurium proximally, invests the capped segment of the nerve. Nerve fibers are numerous central to the cap but within it, they decline in number rapidly so that the tapered end is composed mainly of strands of Schwann cells, macrophages and occasional patches of fibrous tissue. Some fibers have become tangled or turned back but most appear to have remained straight to their blind ends under the cap.

The effectiveness of the method resulted both from the fixing action of the acetone solvent and from the blocking action of the fluid-filled space con-

fined within the hardened plastic, into which nerve fibers will not grow.[3] When a nerve end is coated with the methacrylate solution, the outer surface of the cap hardens rapidly and this retards the evaporation of acetone from the plastic directly adjacent to the nerve. Since acetone coagulates proteins and causes rapid dehydration, the capped nerve segment is quickly killed and fixed.

To test whether sufficient acetone is retained in such a cap to fix a segment of normal nerve completely, the following experiment was performed: A normal sciatic nerve was exposed and ringed with plastic for a distance of 3–4 mm. After 3 days, it was removed and studied histologically. The sections showed that the entire nerve stretch distal to the plastic was in Wallerian degeneration, while in the zone that had been coated with methacrylate, and thereby fixed, the axons were fully preserved.

Combining the important features of mechanical and chemical procedures previously described, the plastic cap is a simple, but reliable, method for preventing the regeneration and reconnection of nerve fibers, as well as the formation of terminal neuromas. Regenerating fibers penetrate the acetone fixed region, though in greatly reduced numbers, and their growth is so impeded that even after one year, their combined volume is still less than that of the fibers originally fixed.

These results pertain to nerves up to 1.5 mm. in diameter and further tests must decide whether the method is equally effective in larger nerves. A preliminary study of sections of a cat sciatic nerve that had been capped with methacrylate showed that the epineurium acted as a barrier to the penetration of acetone and that the best fixation occurred at the cut surface of the nerve. This indicates that the epineurium should be stripped back before capping to expose the nerve to the direct action of the fixative.

SUMMARY

In experiments on transected rat nerves (up to 1.5 mm. in diameter), an effective method was developed for the prevention of fiber regeneration and the formation of terminal neuromas in the proximal stump. The method consisted of capping the distal 3–4 mm. of the stump with a 10 per cent solution of methylmethacrylate in acetone. The acetone fixed the capped nerve segment completely, rendering it relatively impervious to regenerating fibers for periods up to one year. After hardening, the plastic caps became firmly adherent and blocked the few fibers that regenerated into them. Neuroma formation was never observed and the nerves tapered gradually to their blind ends.

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EARLY NERVE AND BONE REPAIR IN WAR WOUNDS

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THE DESIRABILITY of early repair of nerve injuries has been emphasized recently by Coleman,[1] Elkington,[2] Spurling,[3] and Young.[4] We wish to record some of our experiences with war wounds in which there has been combined nerve and bone damage, and in a few of which we have attempted early repair of both lesions.

At the beginning of the overseas activities of our forces in Africa, the treatment of both bone and nerve injuries was conservative. As the campaign progressed, and greater experience in the handling of war wounds accumulated, more radical procedures were carried out in a variety of conditions. Early secondary closure became routine policy, reaching its peak in the Spring of the Italian campaign. At the same time, the bugaboo of infection had been largely dispelled by adequate surgery, with the help of chemotherapy, so that early definitive repair of compound fractures became possible. Coincidentally, early nerve suture became more common. The policy of adequate debridement, loose packing of the wound, followed by secondary closure and definitive surgery within a short period is now definitely established. Although there have been some isolated instances where definitive surgery of extremity wounds has been done at the time of initial debridement, it is believed that this is a needlessly hazardous procedure.

A large percentage of all compound fractures of the extremities are associated with nerve injury. Of 143 fractures of the humerus treated at this hospital in Italy, approximately 30 per cent were associated with radial nerve paralysis. Not all of these nerves were severed and many recovered spontaneously. We believe that it is advisable to visualize all paralyzed nerves at the time of definitive care of the fracture, unless there is a specific note from the forward hospital assuring us that the nerve is intact.

Disability due to nerve paralysis will persist long after the fracture is healed. Accordingly, the plan of therapeutic attack must include a dominant role for the neurologic component of the wound. In many wounds, particularly those caused by high velocity missiles, there is severe comminution of bone: in some instances there is marked loss of bone substance; and in those associated with nerve injury, a considerable loss of nerve continuity may exist. In cases where there has been relatively little loss of nerve tissue, nerve repair can be done without too much difficulty after mobilization of the proximal and distal segments, or following customary maneuvers of nerve transplantation, or flexion of adjacent joints.

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REPAIR OF NERVE-BONE INJURY WITHOUT SHORTENING

The following case report is given briefly, to demonstrate early definitive treatment of a combined bone and nerve injury without much loss of continuity.

Case 1. A French-Arab soldier suffered a perforating rifle bullet wound on 31 January 1944. On admission to the 9th Evacuation Hospital (U. S. Army), he was found to have a compound, oblique fracture of the left humerus with complete radial nerve paralysis. The wounds of entry and exit healed promptly. On 21 February 1944, operation was performed by Lt. Col. James E. Thompson of the 9th Evacuation Hospital and one of us (H.G.S.). The humerus was fixed by two screws, without shortening. The radial nerve was dissected free, mobilized proximally and distally, and 1 inch of scarred nerve was resected. Formal neurorrhaphy was carried out with silk sutures. At that time, no material for creating a protective cuff around the nerve was available. The nerve was laid in a fresh bed, separated from the shaft of the humerus, and the wound was closed. The patient received no sulfa drugs locally or otherwise. Penicillin was not available then. Sutures were removed on the eighth day, with primary healing. On 15 March 1944, the patient was evacuated to Africa.

NERVE-BONE INJURIES REQUIRING SHORTENING

Cases in which there has been extensive bone and/or nerve loss present a somewhat more complicated problem. Yet, here too, an attempt has been made to give early, effective treatment. In wounds of the lower extremity, great loss of nerve continuity can be made up by mobilization and flexion. In the case of the radial nerve, however, large defects cannot be overcome. Shortening of the humerus to permit nerve suture is not a new concept. Coleman[1] states that he carried out some humerus shortening procedures at the Cape May Nerve Centre in 1918. We believe that, where indicated, bone shortening with fixation of fragments has a place in early definitive care, with resulting facilitation of nerve suture. Thus far, we have had occasion to perform radial nerve repair in three cases in which the nerve was prepared at the time of bone shortening and fixation. In all of these cases there was comminution, and in one there was bone loss of 2 inches. In none of the cases were there untoward postoperative complications. The first patient was operated upon in Italy, and the case is presented in some detail.

Case 2. A 23-year-old American soldier was wounded on 28 August 1944, sustaining a compound, comminuted fracture of the right humerus, at the lower portion of the middle third of the shaft, with complete radial nerve paralysis. He was debrided at the 59th Evacuation Hospital (U.S.) about 24 hours after injury, and admitted to the 21st General Hospital on 2 September 1944, with the arm in a shoulder spica. Penicillin therapy was begun on 4 September 1944.

On 6 September 1944, first-stage definitive operation was performed (Fig. 1). The oblique wound of the lateral border of the arm was lengthened proximally and distally. The radial nerve was visualized and found to be torn for 1 inch in length, its severed ends being held only by a thread of shredded nerve sheath. The comminuted fragments of the shaft of the humerus were removed and the humerus was shortened for about 1 inch in its lower third, the bone ends being fixed by a 4-hole stainless steel plate, with an oblique screw for additional fixation. The proximal and distal ends of the radial nerve were then approximated with a single silk suture (through obviously damaged tissue). A single sheet of fibrin film was then wrapped in a cuff around the nerve, separating it from the bone and plate, and the wound

was closed in layers. A hanging cast was applied. Subsequent x-rays showed the fragments of the humerus in good position and alignment.

A window was cut in the cast to remove the sutures. The wound healed *per primum* except for one small unepithelialized area. On 22 September 1944 (25 days after wounding), formal nerve repair was done (Fig. 2). The S-shaped wound was excised. Incision was made along the

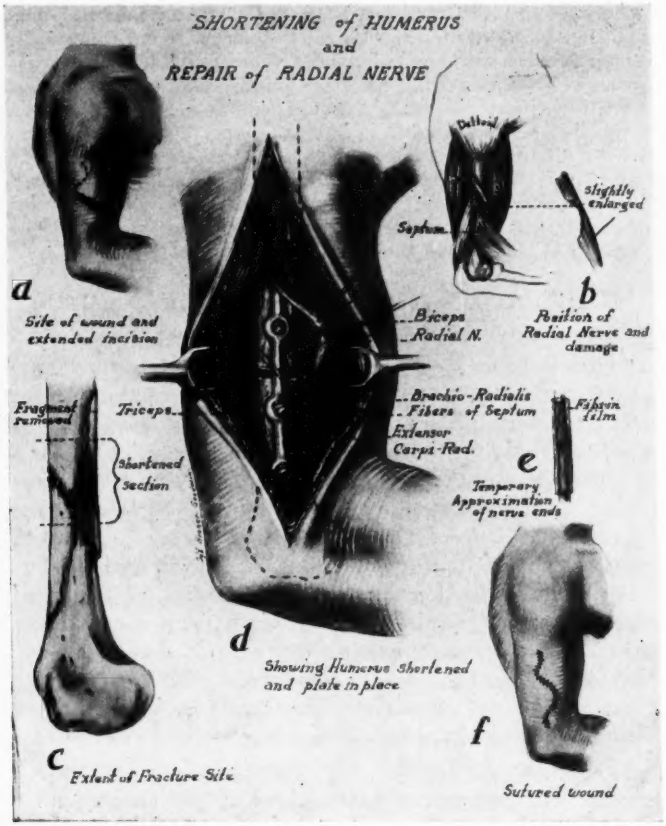

FIG. 1. Case 2. Sketch of first-stage operative procedure. Comminuted bone fragments are removed. The humerus is shortened and fixed with 4-screw plate, plus additional oblique screw. The radial nerve is approximated by a single sling stitch placed through damaged ends, and wrapped with fibrin film.

previously sutured lateral intermuscular septum, continuing down the proximal 2 inches of the brachioradialis muscle. The sheet of fibrin film that had been placed around the nerve was lifted out in one piece. There were no adhesions between it and the outer covering of the muscle, or between it and the enveloped nerve. The portion of the nerve that had been protected by film was freely movable and was covered with a thin, smooth, velvety membrane, completely surrounding the area. This portion of the nerve included the site of the previously placed approximation suture, keeping the cut ends in continuity. It was completely free of

adhesions except for one small point medially, where the film had uncoiled and had not protected it; here there was a band of scar running to the smooth fibroblastic covering of the bone plate (Fig. 2-*a*). It was obvious that in this region the covering of the bone plate had also benefited by insertion of film between it and the nerve, leaving a smooth, non-adherent surface. Proximal to the protected area, there was dense scar between the plate and inter-

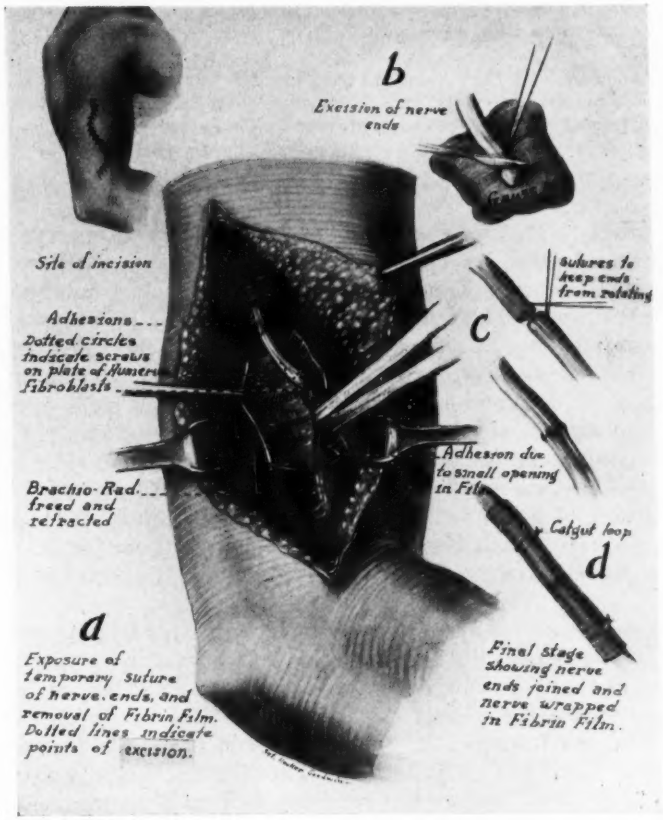
b
Excision of nerve ends
Site of incision
Adhesions
Dotted circles indicate screws on plate of Humerus
Fibroblasts
Brachio-Rad. freed and retracted
sutures to keep ends from rotating
C
Adhesion due to small opening in Film
Catgut loop
d
a
Exposure of temporary suture of nerve ends, and removal of Fibrin Film. Dotted lines indicate points of excision.
Final stage showing nerve ends joined and nerve wrapped in Fibrin Film.

FIG. 2. Case 2. Sketch of second-stage operation. Fibrin film is removed from around previously approximated nerve ends. Scar tissue is present above and below the area protected by film, and one band is seen running from nerve to covering of bone plate through a defect near the lower end of the film. The nerve is dissected free from scar and mobilized proximally and distally. After excision of scarred ends, formal neurorrhaphy is done with interrupted silk sutures. The nerve is then wrapped in a cuff of fibrin film and wound closed.

muscular septum through which ran the proximal portion of the nerve. The difference in the two areas was striking. The proximal portion of the nerve was dissected free of scar and mobilized as it curved behind the humerus. The distal part of the nerve was mobilized down to its course through the supinator. To get adequate length it was necessary to sacrifice a fine branch to the brachialis muscle. Following mobilization, stay sutures were placed and proximal and distal ends of scar were resected, until healthy nerve was reached. Together with

the original 1-inch loss of continuity, this resulted in total loss of about 2½ inches. Bleeding from cut ends of nerve was controlled with saline. Due care was taken to approximate similar fascicular groupings at both ends. With tension maintained by temporarily crossed stay sutures, formal neurorrhaphy was then done with interrupted epineurial sutures of silk. Stay sutures were removed. At the completion of suture the nerve moved freely from side to side. Fibrin film was then rolled around the nerve for 1½ inches on either side of the suture line, its coil being maintained by two fine catgut loops, tied loosely to prevent constriction of nerve. The wound was then closed in layers with silk. The plaster cast was replaced with the elbow in flexion.

On 24 September 1944, the patient was transferred to await evacuation at a neighboring hospital. A letter received from Major J. L. Thomson, dated 20 November 1944, stated that his subsequent course was uncomplicated, and that the patient had then been evacuated to the Zone of Interior. Further word has not been received from the patient.

COMMENT

In addition to the two cases of humerus-radial nerve injury, presented above, we have treated two other patients by shortening procedures followed by nerve repair. No complications have arisen during the time these patients were under our care. There are four points that bear brief discussion, i.e., possibility of infection, time for repair, technique, and end results.

In our experience with internal fixation of compound fractures of the humerus the risk of infection is slight. In one of the four cases mentioned in this report, a superficial infection developed, limited to 2 cm. of the wound after first-stage procedure, and followed by primary healing after the second stage. We feel that the arm is an ideal site for internal fixation of the fracture site and closure of the wound. The excellent blood supply through muscle, and the ease with which bone and fixation material can be covered with muscle account for the uniform success in manipulating and closing these wounds.

In a large number of cases of early bone fixation, without nerve injury, infection has been negligible since the advent of routine penicillin on the Orthopedic Section. On the other hand, in a group of approximately 40 nerve operations performed at this hospital in Italy, only one superficial infection was encountered and that occurred in the single individual who received penicillin. That penicillin alone is not the sole factor is obvious from the fact that in Case 1 the patient received no form of chemotherapy whatsoever. We believe, however, that with penicillin fortification, more radical and earlier definitive surgery can be carried out.

With regard to time for repair, the Orthopedic Section of this hospital has found that secondary debridement, with fixation of compound fractures (where indicated), can be readily carried out within the first 5 to 14 days after injury. Observations by the Neurosurgical Section on nerves seen at the time of secondary wound closure from 5- to 12-day intervals has led us to believe that the condition of the nerve at this time is not conducive to successful repair. Accordingly, in cases of combined bone-nerve injury, we have followed the plan of doing the necessary orthopedic procedures first, and follow with neurosurgery after an interval of 3 or more weeks from wounding.

Tantalum wire sutures and tantalum foil have not been available to us thus far. Undoubtedly, the results with this technique, as described by Spurling, are excellent. Lacking tantalum foil we have used fibrin film, which was made available to us by Lt. Col. John A. Stewart. On gross examination, we have found that its use results in a smooth, non-constricting bed for a period of at least 5 weeks. One of us has had occasion to perform formal nerve suture as late as 5 weeks after initial preparation of the bed. At this time there was no trace of the original cuff of film, but the protected nerve lay free in a smooth bed. Histologic studies of specimens removed by us have not been completed, and it may well be that, after lapse of time, constricting fibrosis does occur.

Fixation of the fracture site at the time of the first operation can be done with either plate, screws, or wire loops. In Case 2 a plate was used for fixation. This is done in cases where the bone is already denuded of periosteum and further stripping is unnecessary in order to apply the plate. If the periosteum is intact, we prefer to use wire loops and immobilize the humerus in a plaster shoulder spica.

We are unable to present any end results of nerve function in the cases that we have mentioned. Some patients have been operated upon too recently, and others have not reported by letter. There is, of course, a possibility that untoward sequelae may develop later. However, our experience to date with internally fixed fractures without nerve injury, and nerve injuries without fractures that have been repaired early, leads us to believe that this is improbable.

It is our opinion that the principle of early bone-nerve repair is worthy of consideration if facilities are available; and that where bone shortening is indicated, deliberate resection and fixation as a planned prelude or accompaniment to formal nerve suture can give the patient a better prognosis. In all such cases, the close cooperation of the orthopedist and the neurosurgeon is essential.

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THE ANTIGENICITY OF BOVINE THROMBIN: CLINICAL EVALUATION

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THE RECENT RISE to importance of thrombin as a hemostatic agent has precipitated a real though largely unpublished debate on the subject of its antigenicity. Two incidental and unrelated factors have tended to promote division of opinion. On the one hand the tremendously rapid strides made in the purification of beef thrombin by the Iowa group under the leadership of Seegers, followed by proofs of its usefulness in surgery, have outdistanced research in the subsidiary problem of antigenicity. On the other, the collection of large quantities of human blood by the Red Cross for the benefit of the combat troops has afforded, in connection with its conversion to serum albumin, an abundant though temporary supply of human thrombin, the superiority of which has been championed by the Harvard group which sponsored the program of blood fractionation. The gulf between those who hold beef thrombin harmless in its surgical application and those who imply danger in the use of thrombin from any source except human blood remains unbridged by a connected line of evidence, and at best has been only sampled.

Antigenicity is a titanic problem handicapped by an interdiction against free transfer of animal evidence into human conclusions, and by a wide personal choice of values ranging from the scientifically absolute to the clinically tolerable. In this paper I shall do no more than to marshall the available evidence, add a new sampling, and reach an obviously temporary opinion. The question of the safety of animal thrombin, however, is of the moment: the cancellation in large part of the production of serum albumin resulted unavoidably in reduction of the by-products from which up to now human thrombin has been derived; the philanthropic nature of the blood collections by the Red Cross prevented the distribution by sale to civilian users; and surgeons therefore are giving increasing acceptance to the clotting agents derived from animal sources, such as bovine thrombin and rabbit clotting globulin, which have now been released by the National Institute of Health for commercial distribution. The case against bovine thrombin will be considered first.

POSITIVE RESULTS IN THE EXPERIMENTAL FIELD

1. EXPERIMENTS OF DR. BEATRICE CARRIER SEEGAL

There are no reports in the literature indicating that sensitization has been produced by injections of bovine thrombin, but immunologists affirm generally that thrombin, being a protein, under favorable experimental con-

ditions should provoke antigenicity of some degree. A series of experiments done by Dr. Beatrice Carrier Seegal yielded successful sensitization of guinea pigs and rabbits to bovine thrombin. She has kindly communicated to me her experiments which may be summarized as follows:

Sensitization of Guinea Pigs. Eleven guinea pigs were injected subcutaneously with 0.5 or 1.0 mg. of alum precipitated bovine thrombin. Four weeks later, 6 of these animals were injected intravenously with 0.6 or 1.0 mg. of the thrombin in solution, given slowly over a period of 30 to 40 seconds in the foot vein. All 6 animals died within 3 to 4 minutes, showing the respiratory difficulty, the cyanosis, and the edema of the lungs typical of anaphylactic shock. The remaining 5 animals, after reactionless injections with human thrombin, likewise succumbed when bovine thrombin was injected. In addition to the 11 animals thus sensitized by subcutaneous injection of an alum precipitated bovine thrombin, 3 animals (weight 350 to 400 gm.) were sensitized by intravenous injection of 1.4 to 2.0 mg. of thrombin in solution and tested for sensitivity 4 weeks later by the intravenous injection of 1.0 mg. of the antigen. Two of these animals died of anaphylactic shock, and the third showed symptoms of moderate shock with a drop in temperature of 1.8°F.

Sensitization of Rabbits. Three rabbits were injected intravenously with a total of 9 mg. each of alum precipitated bovine thrombin over a period of 24 days. Six days after the last injection a sample of blood was drawn from each animal. The serums were tested for precipitins with two lots of bovine thrombin and one lot of human thrombin, diluted 1–500 and 1–5000. All 3 serums strongly precipitated with both dilutions of the bovine thrombins. A trace of precipitate occurred between human thrombin 1–500 and the serum of one rabbit. On the 7th day, the 3 sensitized rabbits were injected into the left cerebral area with bovine thrombin in amounts of 0.6, 0.4 and 0.4 mg. respectively in 0.3, 0.2 and 0.2 cc. physiological saline. Three normal rabbits were each similarly injected with 0.6 mg. of bovine thrombin in 0.3 cc. saline. The sensitized animal receiving the larger dose and 1 normal rabbit, $1\frac{1}{2}$ to $2\frac{1}{2}$ hours later, began circling to the right and falling to the right side, and both animals were dead the following morning. The other two sensitized animals showed clonic right-sided movements (and less active twitching on the left) beginning the day following injection and persisting until sacrifice at 3 days. At autopsy both of the rabbits that died at 20 hours showed slight gross increase in the size of the left cerebrum. One sensitized animal showed a centrally located area of hemorrhage and softening about 7 mm. in diameter, and this proved microscopically to contain nerve cells undergoing ischaemic necrosis, in addition to hemorrhage, oedema, and leucocytic infiltration—the "Arthus phenomenon."

A second type of rabbit experiment was done by replacing the anterior chamber fluid of the eye with 0.4 mg. bovine thrombin dissolved in 0.2 cc. physiological saline. Four weeks later an intravenous injection of 3.5 to 4.0 mg. of bovine thrombin in solution brought death from anaphylactic shock to 1 out of 7 animals thus tested.

Important as these experiments are, certain conditions should be noted: a) The amount of material injected to produce shock was one-quarter to one-half the amount that had produced reactions in unsensitized animals; for example, a normal 208-gm. guinea pig died ten minutes after the rapid injection of 2.0 mg., while the remaining control animals, receiving 1.4 to 2.0 mg. by slow intravenous injection, showed temporary respiratory increase following injection. Likewise, a rabbit receiving 3.5 to 4.0 mg. of thrombin intravenously in the course of 4 minutes, died of intravascular clotting, and the injection time had to be prolonged to 10 to 20 minutes to permit survival by the rest. b) The potency of the solution of thrombin used intravenously is given as 100 Iowa units[13] per mg., but the strength of the alum precipitated

material is not recorded, nor is mention made of the nitrogen content. c) The potency of the human thrombin supplied by the Harvard Medical School that was used to detect cross-sensitization was unknown to Dr. Seegal. d) On the basis of maximum non-lethal doses of 2.0 mg. given to a 250-gm. normal guinea pig, the comparable dose in the 70,000-gm. human being would be over 500 mg. or 50,000 Iowa units of bovine thrombin.

2. EXPERIMENTS OF DAVIDOFF ET AL.

The significance of the experiments to neurosurgery is augmented by a group of studies done between 1931 and 1942 concerning the local sensitization of the brains of animals. Davidoff, Seegal and Seegal[5] demonstrated that a local allergic reaction can be produced in the brain of the rabbit by repeated cerebral and intravenous sensitizing injections of an antigen (red blood cells, horse serum, egg albumen) followed by intracerebral re-injection of the same antigen. Clinical symptoms of varying degrees of severity appeared, referable to the site of injection, and were often followed by death of the animal. The pathological picture in the brain was interpreted as the homologue of the Arthus phenomenon seen in the skin.

To afford more prolonged and intimate contact of the antigen with a local area of the brain, Davidoff and Kopeloff[2] inserted in a cavity cut in the motor cortex a cube of agar jelly containing horse serum, and fortified this sensitizing implant by simultaneously injecting horse serum intravenously. Two to 4 weeks later a "shocking" dose of the antigen was given intravenously, which produced generalized anaphylaxis and, in addition, transient hemiparesis. The experiments were pursued[3,4] with the addition of egg albumen as an antigen, and it was found possible to layer both antigens upon uninjured cortex, horse serum on the left and egg albumen on the right, and produce hemiparesis at will by intravenous injections of the separate antigens, the weakness occurring invariably on the side contralateral to the implanted substances. Some Jacksonian convulsions occurred and occasionally death.

On advancing another step in the animal kingdom, these investigators proved, first, that anaphylaxis can indeed be produced in the monkey (hitherto thought impossible) if sufficient quantities of antigen are employed, although fully sensitized animals showed no evidence of precipitins at the time of fatal shock; and, second, that in monkeys sensitized by the intravenous route the application of the antigen by repeated or continuous contact with the brain results in contralateral weakness, Jacksonian seizures, or death.[8] Injected antigens produced severe Arthus-like reactions of the brain, with local swelling of the hemisphere and aseptic necrosis, the pathological details of which were given in a later report.[6] It may be added that the rhesus monkey, sensitized by repeated injections, was later found to develop precipitins both to horse serum and to egg white.[9] With refinement of technique, the immunological cortical stimulus became a successful experimental tool in the study of epilepsy.[7]

NEGATIVE EVIDENCE OF SURGICAL TRIALS

1. REPORTS OF TIDRICK, SEEGERS AND WARNER

The thrombins prepared from rabbit serum and from bovine serum (as well as from human blood) have been utilized as clotting agents in clinical surgery, and reports on these substances, totalling about a dozen, were consulted to learn if reactions of any sort have been detected. In only one series however, was attention paid to antigenicity, although absence of direct toxicity was mentioned by several.

In a series of 225 surgical cases[14] beef thrombin was used as a hemostatic agent, and a portion of this series together with additions was restudied with special reference to the use of thrombin in skin transplantations in 122 operations done in 53 patients.[15] The latter report is especially valuable, since the skin is an excellent proving ground for antigenicity, and for the further reasons that thrombin of high potency (1,000 Iowa units per cc.) was used, the material was spread upon relatively large areas, and applications were often repeated in the same patient at intervals of many weeks—a combination of circumstances conducive to sensitization. In no instance, however, was there any suggestion of the development of hypersensitization.

To this may be added my experiences, first in an animal experiment designed to simulate surgical conditions and, second, in a clinical series.

2. AN EXPERIMENT ATTEMPTING TO PRODUCE ANTIGENICITY IN MONKEYS BY REPEATED IMPLANTATIONS OF GELATIN SPONGE SOAKED IN BOVINE THROMBIN

Six *Macacus rhesus* monkeys were used in this experiment in which implantations of thrombin-soaked gelatin sponge were made,[11] just as in clinical surgery in the control of hemostasis. The animals were tested at later dates for the development of the precipitin reaction in the blood serum, and for the reaction of the brain to an injection of the antigen. To improve the chances of a positive result two alterations were made in customary surgical procedure: a) the concentration of the thrombin solution was made 1,500 units (Upjohn*) per cc. as against about 100 units believed optimum for hemostasis when using the absorbable matrix technique; and b) multiple implantations (2 or 3) were made upon the same tissue at intervals of 3 days.

An informal canvass was made among several immunologists to determine the most favorable interval for development of sensitization to bovine thrombin, but the answers varied and a graduated schedule, therefore, was set up covering the period between 15 and 45 days after the last surgical operation. Details of the experimental calendar are given in Table I.

Operative Procedure. General anesthesia was used (cyclopal, 100 mg. per kg. body weight, intraperitoneal). The scalp was clipped, shaved, and prepared with soap, ether and mercresin.

* A single standard for the measurement of clotting activity has not yet been agreed on. The Upjohn unit[1] is roughly one-third as potent as the Iowa unit. Henceforth in this paper the Upjohn unit is implied since the thrombin used was an Upjohn research preparation.

Midline incision made. Cranium perforated and rongeured away to expose the superior sagittal sinus. Sinus opened by an incision about 6 mm. long. A piece of gelatin sponge, cut 5 × 10 × 10 mm. and soaked in bovine thrombin, 1,500 units per cc., was laid across the opening in the sinus to secure hemostasis. It is estimated that 150 to 200 units of thrombin were embodied in the resulting clot. The wound was then closed in layers with silk. Three days later the wound was reopened, the pledget of gelatin sponge was peeled off the dura, bleeding was reinstigated, and a new piece of sponge laid down to effect hemostasis; the wound was then closed. Again 3 days later the wound was reopened, and the process repeated.

It was my hope to prepare 6 animals in this manner. However, one died soon after the conclusion of the third operation; another was considered strong enough only for two operations, and one developed a wound infection following the second operation which, though held in check by penicillin, prohibited further surgical exposures. Despite these inadequacies 5 animals contributed to the experiment, as indicated by Table I.

Bleeding for precipitin tests occurred just before the third surgical implant, just before the intracerebral injection, and at sacrifice. Six tubes, each containing 0.5 cc. serum, were layered with the antigen in dilutions 1–10, 1–100, 1–1,000, 1–10,000 and 1–100,000. The 1–10 failed to result in a good layer, but the rest were satisfactory. Tests were incubated at 37°C. for 1 hour, observed for ring formation, then refrigerated overnight and observed again.

Each animal was tied to a board for an hour in advance of the intracerebral injection and kept there for 3 hours following, record being made of the

TABLE I. *Calendar in days showing the schedule of surgical operations, intracerebral injections of the antigen, and sacrifice for 5 Macacus rhesus monkeys.*

Monkey No.	Surgical Implants			Injection	Sacrifice (days after injection)
	1st	2nd	3rd		
56	0	3	—	15*	3*
57	0	3	—	15*	3*
58	0	3	6*	24*	3*
54	0	3	6*	32*	3*
53	0	3	6*	45*	3*

* Blood serum tested for precipitation with bovine thrombin in dilutions 1/10, 1/100, 1/1,000, 1/10,000 and 1/100,000. *No positive tests.*

pulse, respiratory rate, and temperature. The injection consisted of 0.1 cc. of sterile distilled water containing 10 units of thrombin given through a 25 g. needle inserted 10 to 15 mm. into the right cerebral hemisphere. The amount of thrombin injected contained approximately 1 mg. of solids. The lot analyzed 4.96 per cent nitrogen.

Results. The precipitin tests were negative throughout. The injection of the antigen into the brain failed to cause any observable change in the behavior or appearance of the animals, or alteration of the trend of the pulse, respiratory rate, or temperature. The animals remained normal during the

three-day interval before sacrifice. The implantation sites failed to show reactions different from those produced by a single implant,[11] and the reaction in the brain to the injection was only that which would be expected from the mechanical trauma of the needle insertion. The Arthus phenomenon was not seen.

3. PRECIPITIN TESTS IN 15 PATIENTS IN WHOM BOVINE THROMBIN WAS USED FOR NEUROSURGICAL HEMOSTASIS

In a group of patients in whom bovine thrombin had been used in the course of routine neurosurgical operations (see Light and Prentice[11] for types of procedures), precipitin tests were done on those willing to submit to

TABLE II. *Thirteen patients submitting to precipitin tests following surgical operation at which bovine thrombin was used as a hemostatic agent, implanted on pieces of gelatin sponge.*

No. of Hemostatic Patches Laid Down	Thrombin: Units (Upjohn) per cc.	Precipitin Tests	
		Post-oper. Interval in Days	Result
1	300	194	Negative
3	100	130	Negative
2	300	128	Negative
6–8	50	121	Negative
8–10	50	100	Negative
5–6	100	79	Negative
2	100	77	Negative
6–8	100	70	Negative
1	100	54	Negative
1	100	42	Negative
4	100	37	Negative
10–12	100	11	Negative
3–4	100	10	Negative

TABLE III. *Precipitin tests with bovine thrombin as the antigen, done on two patients who had undergone multiple operations at which bovine thrombin was used as a hemostatic agent.*

Sex	Age	Dates of Operations	Interval between Operations	No. Pieces Implanted	Units per cc.	Precipitin Tests	
						Weeks after Last Oper.	Result
F	45	2/2/45 2/21/45	19 days	1 8–9	100 100	7	Negative
M	26	12/27/44 1/11/45 2/26/45	15 days 46 days	3 4 3	100 100 100	2, 3, 5, 7, & 1	All negative

collection of blood serum, using the laboratory procedure outlined above in connection with monkeys. Tables II and III give the results.

Only crude estimates can be made of the total amount of thrombin permanently deposited in the body during hemostasis, but it appears to have approximated from 5 to 10 units for each piece of gelatin sponge implanted when the solution was made up to contain 100 units per cc. The values of implanted thrombin therefore range from 10 to 120 units.

There were no positive results of the precipitin tests.

DISCUSSION

While the brief experiences of clinical surgery do not constitute an adequate endorsement of bovine thrombin, nevertheless they offer assurance that the likelihood of sensitization is small in connection with the use of the material in routine surgery. That view gains support from an experiment of slightly increased severity done in monkeys, again representing, however, the surgical side of the case and not sound immunological technique. Whether in surgery the situation may ever arise in which the rigid sensitization procedures that have been applied successfully to guinea pigs and rabbits are duplicated, is a matter of conjecture. Presumably that will not occur.

One may speculate with interest on the position ultimately to be assigned to thrombin among the antigens. Pure thrombin has not yet been prepared and studies of antigenicity are confused to some extent by reactions to the contaminating proteins. The question naturally arises: when purity is achieved, will thrombin be found to possess species specificity or group specificity? The answer has already been determined with respect to its activity as a coagulant of the blood, for the thrombins of the mammalian series are alike, but differ from those of birds and those of amphibians.[12]

In the case of insulin both hormonal activity and antigenicity are drawn upon the basis of group distinction rather than of species.[10] The danger of sensitization is from insulin itself, not from the parent animal substances. By comparable reasoning, the possibility exists that an animal can be sensitized to the thrombin derived from any species of the group including its own, a possibility made all the more valid by the presumption that thrombin is not a normal constituent of the blood. If this is true, the question of safety is one of quantity (modified by individual susceptibility), in which case experiments concerning actual surgical use become definitive.

CONCLUSIONS

1. After the surgical use of bovine thrombin in hemostasis, *Macacus rhesus* monkeys failed to develop either precipitins in their blood serum, or any local tissue reaction in the brain (Arthus phenomenon) upon injection of a small amount of the antigen.

2. In 15 patients precipitin tests done from 10 to 194 days following the neurosurgical use of bovine thrombin as a hemostatic agent yielded no positive reactions.

3. While bovine thrombin may be employed in surgical hemostasis with

relative safety from sensitization, much more precise knowledge is required to establish the limits of safety and the basic position of thrombin among the antigens.

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EXTRADURAL PNEUMATOCELE FOLLOWING TANTALUM CRANIOPLASTY

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THE REPAIR of cranial defects caused by war wounds of the head, by the use of the element tantalum has evolved as one of the major contributions of rehabilitation neurosurgery.[4,5,7,8,12,13,16] The clinical use of tantalum as a cranioplastic material was based upon a reasonable foundation of experimental trial and, in particular, there appeared little doubt from these studies that this substance was relatively inert in tissue. A fine, relatively non-progressive connective-tissue encapsulation or reaction does develop in tissue exposed to tantalum,[1,2,3,9,10,11] and this histologic change is well known to military neurosurgeons experienced in its use. Certain unpublished data exist that suggest an absence of any significant reaction in patients or in experimental animals to extremes of heat, cold and electrical fields. There has been no clinical report of an untoward reaction in a patient to such potentially noxious stimuli or adverse influences.

Together with certain as yet ill-defined fears for a valuable procedure in which much thought for the well being of the patient has been invested, the military surgeon is more concerned immediately with the possible complications of tantalum cranioplasty that must be faced in the early period after operation. There is little doubt but that a delayed type of wound infection involving the extradural extent of the cranioplasty is the one most frequently encountered. Case 1 described in a previous discussion of this subject[7] developed an infection ten months after tantalum cranioplasty and several months after discharge from the Army. The plate was removed by the attending surgeon. It is of some interest that the original injury was followed by cerebral infection and the development of a cerebral fungus. A second case in another series[16] had developed a spreading bifrontal infection four months following injury and prior to a cranioplasty that had been controlled by surgical drainage and parenteral penicillin therapy, with the incidental removal of a mass of silk suture material from the region of the original debridement. After insertion of a massive frontal tantalum plate, a second infection occurred eight months later. This again subsided after surgical drainage and chemotherapy but with loss of the plate. The "foreign body" quality of tantalum has not as yet been fully established in the three years in which it has been used as a cranioplastic material.

In the course of reviewing skull defect repairs in the Neurosurgical Centers of the Zone of the Interior, one of us (B.W.) has encountered two instances of another and fortunately readily amenable complication of tanta-

lum cranioplasty. This in essence consists of the formation of an intermittent extradural pneumatocele due to the presence of a fistulous tract between the frontal sinus and the thin fibrous envelope that characteristically encloses a tantalum plate. The development of such a grotesque and possibly dangerous complication of alloplastic cranioplasty has not been reported previously, although this may be quite fortuitous or because the reference has not been found. The use of autogenous bone would tend to discourage the existence of the potential space necessary for its evolution, although it might readily

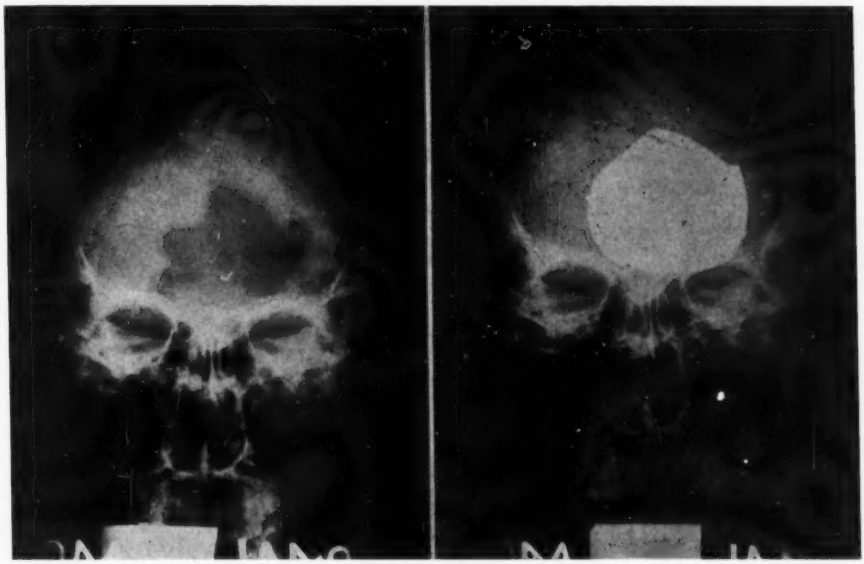

FIG. 1. Case 1. Pre- and post-operative roentgenograms of skull demonstrating involvement of frontal sinuses.

occur if celluloid were used as the cranioplastic material. Alloplastic cranioplasty involving a mastoid cell might conceivably be followed by the same sequence of events. The clinical picture may be protrayed by a brief description of two cases.

Case 1. Walter Reed General Hospital. This patient, whose early clinical course and primary cranioplastic repair has been reported elsewhere,[16] sustained a mid-frontal compound fracture of the skull with cortical laceration as the result of an aerial bomb fragment wound on 27 November 1943. Wound healing after the initial debridement and closure of this lesion was without incident, and the patient was admitted for cranioplasty on 17 June 1944. The procedure was carried out on 6 July. A review of the operative note of that date and numerous photographs that were by chance taken of that particular cranioplasty, fail to show any involvement of the frontal sinus. The pre- and post-operative lateral roentgenograms of the skull reveal, however, an extension of the defect into the upper projection of the right frontal sinus (Fig. 1).

There was a slight bloody discharge from the nose for the first three days after operation and this finding involved the patient in a certain amount of clinical suspicion from the very beginning of his convalescence. The discharge subsided, and under parenteral penicillin the fear of infection or any untoward complication subsided. During the sixth week of his postoperative course, he voluntarily presented himself with the simple complaint that a soft mass would appear in the center of the forehead every time he blew his nose, a finding that was first manifest during the course of a severe coryza. Forced expiration with the nares closed caused the immediate development of a soft, fluctuant, readily collapsible oval swelling directly above the medial half of the right frontal sinus, assuming the shape of the original tantalum plate. The mass was not aspirated since the diagnosis was sufficiently obvious and was at once confirmed by lateral roentgenography.

Operation: 12 December 1944. *Bifrontal craniotomy, removal of tantalum plate, plastic closure of communication between extradural space and frontal sinus, refixation of plate.*

After the usual preparation of the operative field, the former coronal scalp flap was reopened and reflected rostrally, exposing the area of the cranioplasty. The external surface of the tantalum plate was covered with a thin, translucent film of connective tissue, under which there was a large pool of air from the frontal sinus communication. The fibrous film was not adherent to the small drainage holes in the plate. This tissue was removed and the tantalum plate released from its fixation points. Along the right lateral margin of the plate, bone tissue had grown over the external surface of the tantalum for a distance of about 3 mm. over an extent of about 2 cm. The former bony ledge was lined with smooth connective tissue and there was no evidence of bone formation beneath the plate. The extradural defect was smooth and glistening and covered also with a translucent membrane closely adherent to the dura. There was an extradural defect then between the dura and plate, about $\frac{1}{2}$ cm. in depth. In the right frontal angle of the defect, there was a small oval aperture, about 2 by 4 mm. in size, which communicated with the right frontal sinus. The depth of this sinus tract was gently curetted. A semicircular incision was made in the adjacent pericranium and this flap of tissue was drawn over the aperture and sutured to the dura, effectually closing the communication with the sinus. The plate was then refixed in position with the original tantalum wedges.

Case 2. Kennedy General Hospital. The patient sustained a compound depressed fracture of the right frontal bone and right frontal sinus on 8 October 1944. Debridement of bone fragments and suture of a dural laceration were carried out by an overseas civilian surgeon. Wound healing was normal and he was transferred to an Army General Hospital. Three months following injury the frontal defect was repaired by tantalum cranioplasty. The cosmetic result was satisfactory. The operative note did not explicitly describe the pathologic foundation for the ensuing development of an extradural pneumatocele.

At an undetermined time after cranioplasty, possibly one month, the patient first noticed the development of a well rounded, soft mass in the forehead immediately after blowing the nose. On two occasions, a more diffuse subcutaneous emphysema developed that was painful and did not recede for several days. At the time of reparative surgery, the lesion had become well localized.

Operation: 3 April 1945. "*Operation for surgical repair of fistula between frontal sinus and envelope surrounding tantalum plate.*"

"The scalp flap made at the first procedure was reflected. The tantalum plate was found completely surrounded on its external surface and edges by a well organized, pliable, thin, veil-like membrane of tissue. Its surface opposing the plate was smooth and glistening. It had also grown into the interstices between the tantalum pegs.

"The edge of the organized false membrane was dissected away from the plate and the pegs were withdrawn from their insertion between the two tables of the skull. When the plate was removed, a similar thin glistening film of tissue was found adherent to the dura as well as overlying the frontal sinus. It was intact everywhere except over the sinus, where a circular opening, 2 mm. in diameter, opened into this structure. It was obvious that this opening con-

stituted a fistula between the frontal sinus and the envelope of organized false membrane that surrounded the plate, and that the envelope become inflated by air directly from the sinus (Fig. 2).

"A circular incision, 1 cm. in diameter, was made surrounding the fistulous opening. Two small semicircular flaps, consisting of the outer half of the organized false membrane, were dissected free almost to the opening and imbricated with interrupted sutures. A third flap of tissue, derived from the external layer of the organized membrane, completed this closure.

FIG. 2. Case 2. Operative site after removal of tantalum plate. The arrow indicates the fistula into the frontal sinus. The curvilinear outline of the bed of the tantalum plate is indicated by the elevated ridge of tissue adjacent to the skull.

The original tantalum plate was re-inserted, fixed with new tantalum points, and the wound was closed in layers with interrupted black silk sutures."

There has been no evidence of recurrence in either patient to the present date.

COMMENT

The passage of atmospheric air into the tissues of the cranium and its contents may produce a striking variety of clinical syndromes, whether the etiological agent be trauma, infection, tumor growth or congenital defect.[15] These disturbances may be grouped under the following headings:

1. Emphysema capitis.
2. Pneumocephalus interna.
3. Pneumatocele frontalis externa, or pneumatocele syncipitalis.

4. Pneumatocele supramastoidea.
5. Pneumatocele occipitalis.

The type of extradural pneumatocele described in this report may be considered somewhat analogous to the third type noted, that of pneumatocele syncipitalis or pneumatocele frontalis externa. von Helly[6] originally described this lesion as a more or less encysted collection of air between the skull and the pericranium, located over either supraorbital ridge and caused in the majority of cases by trauma. The mechanism of its development demands a break in the continuity of the outer sinus plate without disruption of the pericranium, and the forceful intermittent passage of air through coughing or sneezing into the potential space thus created, from which the air cannot be absorbed. The analogy fails, however, when it is recalled that the extracranial or extra-tantalum plate mass appears because of the passage of air through the drainage holes in the plate from the fistulous opening beneath the plate communicating with the frontal sinus.

This type of pneumatocele also bears a superficial relationship to pneumatocele occipitalis, first described by Wernher,[14] in which a fistulous tract from the mastoid antrum may extend into markedly expanded cells in the parietal bone and, with extradural and extracranial rupture, present as a globular, collapsible mass in the occipito-mastoid region of the skull.

An effort to relate the particular form of extradural pneumatocele under discussion to these well recognized forms is purely academic, although they have in common the feature of an opening from the external environment into the extradural space. The peculiar tissue reaction to a tantalum plate that results in an envelope of fibrous tissue and the existence of an opening into the frontal sinus, or theoretically into a mastoid cell, sets the stage for the development of this unique pneumatocele.

It is of historical interest that the principle of surgical obliteration of the communication between any type of pneumatocele and the external environment was recognized early, although the methods of compression bandaging, injection of sclerosing substances and the stimulation of infection at the fistulous site can scarcely be commended. Such communications in any type of pneumatocele may be closed by the application of a graft or some simple plastic procedure as that used independently in these two cases.

CONCLUSION

Tantalum cranioplasty has been widely applied in the repair of skull defects caused by war wounds. Although experimental and clinical studies have indicated that this element fulfils many of the essential requirements of the ideal cranioplastic material, a continual appraisal of early and late complications incidental to its use is mandatory. Two instances of extradural pneumatocele have been described which were dependent upon a fistulous tract extending from the frontal sinus into the characteristic fibrous envelope that surrounds a tantalum plate after fixation in a skull defect.

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CLOVIS VINCENT
NEUROSURGEON AND PATRIOT

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"He who cares for patients suffering from brain tumor must bring to his task much thought and stout action. There is need, too, of formidable optimism, for the dice of the gods are ded!" Foster Kennedy.

If this be true in time of peace, security and plenty, how much more' then, must one bring to neurosurgery in a country overrun by a savage destructive enemy? No one can estimate, before the need arises, the extent of one's courage, strength and resourcefulness. It was given to one man, in the course of this war, that all of these qualities be tried. This man is Clovis Vincent, Professor of Neurosurgery at the Faculty of Medicine of Paris, and head of the Neurosurgical Service of L'Hôpital de la Pitié.

Clovis Vincent, spiritual son, pupil and heir of Babinski, of whom the latter said: "When I die I want Vincent to carry on my work. . . ." Clovis Vincent, colleague and friend of Harvey Cushing, with whom he worked in America, friend of Bailey, Peet, Penfield, Cairns, Dott, and del Río-Hortega, brilliant pathologist who came to Paris to work in his clinic—men who in the four corners of the world have had the vision to lay the foundations for that most exacting form of human endeavour, neurosurgery.

His is a story that should be told. In war as in peace, he cherished the highest of medical ideals—the preservation and prolongation of human life. His faith in his ideal carried him through a myriad of difficulties, and gave him the strength to accomplish, almost single-handed, that gigantic task which he set before himself of his own free will—to keep the doors of his neurosurgical clinic open to those in distress throughout the entire German occupation of France. He undertook that task on June 14, 1940, on the day Paris fell, and those doors are still open today.

Sacrificing his health, his home life, his personal means, and forever exposing himself to the savage vengeance of the Gestapo assassins, Clovis Vincent moved into his clinic on that dark day when German troops goose-stepped down the Champs Elysées. He stood by and lived with his patients. He ate the same pitiful food they ate; he slept on one of the hospital cots; he was on call for almost four years without interruption. And on August 23, 1944, when the last of a beaten enemy stole silently away in the night, he was still on duty, caring for those who had been operated on that very day.

Clovis Vincent is a Frenchman and a patriot. All means justified the end, and the end was to fight, to defeat the purpose of an enemy who had not only invaded his country and his hospital, but the very wards and operating

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rooms where he worked. The tales that could be told are numberless. For reasons of military security, many cannot be recounted now. For other reasons, some will never be disclosed. But one that will never be forgotten is the story of Vincent's lecture given to a group of visiting German medical officers.

A few weeks after the German Army had come to occupy l'Hôpital de la Pitié, Vincent was approached by the German C. O. This flattering gentleman wondered whether Professor Vincent would mind lecturing to some of the younger medical officers who had heard so much about his brilliant work in neurosurgery. Professor Vincent regretted that time did not permit him to give a special lecture, but if the young students wished to attend his regular Thursday clinic, they might watch him examine his patients then. The courteous conquerors would be very happy to do so, and they would come on Thursday without fail.

In the meantime, word had spread amongst Vincent's staff of the expected German visitors. It was not without some trepidation that his entire staff—assistants, interns, externs and nurses—crowded into that clinic on Thursday morning. All heads turned to see the visiting gentlemen in green. Very erect, and very smart looking they were, these German medical officers. Some wore short stilettos, the scabbards hanging on the ends of elaborate silk cords; others wore spruce little holsters on their belts. The pistol butts could not be mistaken for syringes. They took their front row places, and all waited in silence.

Tall, erect, white-haired Clovis Vincent walked into the room. Dressed in a white laboratory coat fastened by safety pins, the open collar showing the top of his favorite turtle-necked pullover, the Professor asked that the first patient be brought in.

Clovis Vincent leans over the stretcher, lifts away the sheets and presents his first case:

> This is a child about 4 years old, name and identity unknown, found unconscious on the highways northeast of Paris. Gunshot wound of the head, depressed fracture of the skull, multiple lesions of the cortex . . . .

He gives full details of the emergency operation. The stretcher is wheeled out. He presents the second case:

> This is a woman about 50 years old, name and identity unkown, found unconscious on the highways northeast of Paris. Gunshot wound of the head, depressed fracture of the skull, multiple lesions of the cortex . . . .

He again gives full details of the emergency operation. The stretcher is wheeled out. Vincent leans over the third stretcher and begins:

> This is a child about two years old, found unconscious on the highways . . . .

But the visiting German medical officers have discreetly disappeared. They no longer cared to learn any more about neurosurgery.

This is but a simple tale. Above and beyond this or that incident that makes Clovis Vincent a patriot and one of this war's heroes, there rises an

even greater figure. Of him it can be truly said, to paraphrase a great saying:

> Greater love hath no man than this, that he was ready to lay down his life for the thing he believed in most—neurosurgery.

* * * *

Clovis Vincent's own account of the Clinic of Neurosurgery of L'Hôpital de la Pitié, as it was during the occupation, follows:

We are free again. The Gestapo no longer stalk us. We can look back and speak without worrying about the possibility of immediate dire consequences. We no longer have to think: "Who is in that suspicious looking car driving up and down our street? Are they coming to look me up? What *alibi* must I prepare in order to explain away the mischief I have done?"

I felt certain, from the start, that the English would win in the battle for Britain. The day the Germans entered Paris, I spoke to the Director of the Assistance Publique (State Hospitals) of that period. I had seen him several times in the course of that preceding week in order to discuss my retreating with the French Army. I could not believe that we would not put up a fight on the Loire, flanked as it is by its tributaries and protected by the mountainous regions of the Morvan. That is why I said, "Even if we sign an armistice, England will win." "Why?" he asked. "Because," I replied, "one must have ships to travel on water, and Germany has no ships." Then I added, "France will take up arms again." And I returned to La Pitié.

The following morning the Germans had already sent their wounded to my clinic. They knew, even better than did the medical G.H.Q. of the French Army, that in La Pitié Hospital there existed a department of neurosurgery. A few days later the German doctor who was to become C.O. of La Pitié informed me that I was to remain at the hospital. All of the other heads of departments had been expulsed. I must add that his behavior was irreproachable; he even tried to be friendly . . . . This did not prevent me from refusing to attend the banquet he gave for the German and French doctors on the day of his departure.

At this time, America had not yet entered the war, and the Rockefeller Foundation still had its office in Paris. I wanted to leave France, cross over to England, and join up with de Gaulle's Army as a combatant. I spoke to Dr. O'Brien of the Rockefeller Foundation of my plans. He said, "You must remain here. This war will last a long time. Our civilization is in great peril. Small islands of civilization must be formed. You must form one of these islands." I remained. And for 4 years I lived with the Boches alongside of me. Up to 1942 our relationship was formal. The German doctors called me in on consultation and asked me to operate.

But during all of this time I lived with the thought of secretly resisting the enemy. In December of 1940 the Society of Neurology refused to admit our friend Madame Roudinesco as a member. Ballots had been taken three times in succession, and each time her candidature had been turned down. I protested against this act, called their voting unfair, and wrote to the President of the Society, telling him of my protest. I added that I would not set foot into their meetings until a new era would come. Theirs was a political vote; Madame R. was reproached for being a Jewess.

This was also the period when I turned down an offer to collaborate with a "very distinguished gentleman" who was sent by the Germans to see me. My secretary was present at this interview, and recorded the conversation in shorthand notes, in accordance with my instructions.

"What is it you wish, Monsieur?" I inquired.

"I have been sent by the Collaboration Group to ask you to say a few words on what you think of collaboration. We will record your speech and present it on the air as an interview-broadcast. You will be in good company with Mr. George Claude, etc."

I interrupted immediately and said: "Monsieur, in this world there are not only Germany and France, there is also America, and I must not forget that I owe my chair of Neurosurgery,

created by the Rockefeller Foundation, to the Americans; you must therefore understand, Monsieur, that I will not say anything along those lines."

The man, very embarrassed, fumbled, excused himself, and left saying, "I did not know these details; if I had known them, I would not have permitted myself to come here and bother you."

During this period too, I managed to save from the firing squad a Frenchman who was a magnificent English spy; and hid in my clinic, for almost two and a half years, the Mayor of . . . , whom I got out of prison towards the end of 1940; and, thanks to certificates and numberless maneuvers, gave an Allied agent, Mr. . . . , the opportunity of escaping.

My entire staff knew that I would not admit an armistice that had been decided upon by an old fool, blown up with pride, in a fit of depression and Anglophobia; this old man who believed from as far back as 1917 that France deserved to be defeated. They knew also that I was certain of a German defeat. At that time I said to one of my assistants, Dr. T., who was a friend of Pétain: "Pétain is an old. . . ." He replied, "I will not permit you to speak thus of Maréchal Pétain." I said, "I'll speak thus if it so pleases me."

In 1942, when the direction of Paris passed from the hands of the Wehrmacht to the Nazis, my relationships with the Germans became more strained. First of all, they were afraid of the presence of my clinic right in the middle of the hospital they occupied, and they invited me to leave La Pitié. They said to me: "You have a very busy clinic. Every Thursday and every Sunday hundreds of visitors walk into your clinic. Can you be certain that there are neither Jews nor Communists among them?" "How do you expect me to be certain?" I replied. However, Miret, General Secretary, who showed himself very energetic in his actions, and I discussed this problem and fought hard until we finally obtained authorization to let me move into the Maternity wing of La Pitié. The Maternity clinic had been driven out by the Germans. This building opens directly onto a side street; it was walled off on the side that led into La Pitié. It was in this fashion that the Occupation Authorities thought themselves sheltered from the Jewish and Communistic "terrorists." This word would make them tremble.

It took six months to completely reorganize the clinic. Many patients died because they could not be operated upon. Many records and specimens were lost in the hurried moving, and a lot of our surgical supplies, gowns, etc. were stolen. The moving had one advantage: I no longer saw them, and they no longer asked anything of me. They had received orders to this effect.

Our resistance became more active. All in the clinic knew what was on their chief's mind, though I managed to give the least outward signs of activity in the resistance. Two of my externs were arrested: one was released; I do not know what became of the other. One of my former interns took refuge in the city of Lyons, where he later joined the Maquis; his record with these men of the Resistance is magnificent. He was with E.B. in the V . . . , and it appears, unfortunately, that he was killed. Another assistant, married to one of my former interns, had to flee with her husband. They managed to get across to Africa and at present are in the Army of General. . . . (I am certain that these two pupils of mine were denounced.)

During the last 18 months, when French Resistance became more active and began committing acts against the enemy, the Clinic operated on and made dressings for those who were wounded in their encounters with the enemy. The mistress of one of these wounded denounced us to the enemy. As a direct result, one of my department heads, . . . , this incomparable man, took the blame on himself for these secret treatments. The enemy began hunting for him, but, warned in time, he evaded capture and joined up with the Maquis in the greater Paris area.

We continued to hide Communists and men of the Resistance. One of these, suffering from a skull injury, watched over by the enemy for 8 months, was freed through a coup carried out successfully by his friends. On the day he escaped, my clinic was raided by the Gestapo, and a company of policemen searched the building from cellar to attic.

I was personally chosen as a candidate for the various Resistance Movements Committees. I did not have an important role. I could not. Alongside such leaders as . . . , my part was small. Without them the Resistance would not have been.

But French neurosurgery had to be preserved. And, in my clinic, I was about the only one who could guard it. Neurosurgery, as I see it, imposes the obligation of keeping alive, at any price, the patients one operates upon. And in order to do so, a close watching of these patients must be kept continuously. The war had made my obligations more imperious. We were short of everything needed in our work. At one given time there were only 6 needles in our clinic. The assistants, depressed, distracted by the difficulties of the life we were living, committed errors which were not without consequences. The nurses, poorly paid, undernourished, often ill-treated by the inspectors of the Assistance Publique, sometimes forgot the most elementary gestures and procedures in their work. And mortality increased by 10 per cent. Since the liberation it has fallen back to from 12 to 15 per cent.

Nevertheless, during the last months, neurosurgery came pretty close to sinking. The work of 4 years just missed being destroyed. After the landing in July, because of the increased arrivals of wounded Germans, the German medical high command decided to take over the Maternity building in which we were lodged, in order to put their wounded there. I resisted, inch by inch. Nevertheless the Germans first occupied one-half of the ground floor, then, despite my resistance, took all of the first floor. The patients had to be transferred to La Salpetrière Hospital. At the end of July they wanted to take over the rest of my clinic. I said that I would not leave because I could not leave, that there was no place in Paris that could take me in.

Behind the screens that separated me from the German occupants I kept a bridgehead: 30 beds, the operating rooms, and the radiology department. The Germans could not crowd me out of these. It was from this vantage point that we saw, one night, the departure of the invaders, a departure intended to be secret. And I was able to retake my wards, after having first disinfected them, because pus had flown everywhere.

Reorganization was speedy, and 15 days ago I was able to show to American neurosurgeons, American neurosurgery in France, which I had guarded, because of them, in France.

Clovis Vincent

Paris,
March 30, 1945.

CASE REPORTS AND TECHNICAL NOTES

ANTERIOR SACRAL MENINGOCELE*

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Anterior sacral meningocele is a meningeal cyst which presents anteriorly through a unilateral congenital defect n the sacrum, in contrast to the usual posteriorly situated midline meningocele.

In recent years the condition has aroused increasing interest due to its rarity and to the unhappy complications resulting from incorrect diagnosis and treatment. In their extensive review of the literature Coller and Jackson[1] uncovered 23 cases, of which 18 were treated surgically with a case mortality rate of 44 per cent, and eight patients of this group were cured. Shidler and Richards[2] recently have contributed one additional cure, and this report adds a tenth successful surgical result to the literature. This presentation is intended to aid in standardizing the operative management of this unusual lesion in the light of our own and the reported experience of others.

The procedure of choice appears to be a posterior transsacral approach, excision of the cyst, and ligation or suture of the pedicle. For additional bony protection it is preferable to transfix the pedicle within the sacral canal beneath the most caudally placed intact neural arch. Other adjuncts to the surgical management are closure without drainage, obliteration of the dead space by soft part suture or postoperative elastic pressure, and the employment of prophylactic chemotherapy. The abdominal and the transvaginal routes of approach to expose an anterior meningocele have proven almost uniformly unsuccessful and often fatal. The technique of posterior drainage and packing of a dead space that leads to the spinal theca and opens immediately contiguous to the anus invites disaster in the form of retrograde contamination.

A survey of our own and the available cases in the literature immediately suggests that the presenting symptoms may be developed along three general lines: (1) Local manifestations due to pressure of the cyst on the rectum and adjacent pelvic viscera; (2) neurological deficit in the sacral segments; and (3) disturbances resulting from intermittent increase in intracranial pressure by direct hydraulic action. The size of both cyst and pedicle, the direction taken by the enlarging mass, and the degree to which neural elements are incorporated within the sac are the determining variables. As growth occurs the cyst may enlarge anteriorly, lateral to the rectum, and enter the true pelvis with resulting constipation, menstrual disturbances and, at times, soft part dystocia. Sphincteric disturbances and varying grades of sacral anesthesia are the usual neurological manifestations. Pressure on a cyst (as in sitting) that has a broadly patent communication to the terminal theca will be immediately transmitted to the cerebrospinal system, giving rise to headache, and the usual train of symptoms associated with increased intracranial pressure; whereas, if the pedicle is markedly attenuated this will not be observed.

CASE REPORT

A 26-year-old white female was admitted to the Out Patient's Hospital of the United States Naval Hospital, Oceanside, California, on January 22, 1945. Her chief complaint was severe, aching pain in the sacral region of four years' duration. The pain was intermittent in occurrence, but in recent months had recurred with increasing intensity and radiated into the left sciatic distribution. The discomfort was particularly acute in the sitting position, which could be endured for only 15-minute periods. Associated with sacral pain were episodes

* The Navy Department does not necessarily undertake to endorse views or opinions which may be expressed in the pages of this publication.

of bitemporal headache, nausea, vomiting and photophobia. The patient had been aware of borderline incontinence all her life, with occasional urinary or fecal soiling on laughter or unusual exertion. Her past history was significant in two respects: (1) She had suffered several attacks of pyelitis, and urograms taken elsewhere revealed a coexistent congenital anomaly in bilateral bifid renal pelves; (2) the first pregnancy was stillborn following high forceps extraction, and two subsequent deliveries were carried out by Caesarian section. She dated the onset of sacral pain to the first instrumental delivery four years ago.

Examination. There were no abnormalities in the general condition. There were well-healed Caesarian section scars. Local inspection revealed an aberrantly formed sacrum having a large left-sided bony defect with the intact portion deviating to the right. On bimanual palpation an exquisitely tender, fluctuant mass was outlined occupying the sacral defect and

FIG. 1. Flat x-ray film of the lumbosacral spine and coccyx taken during urographic studies shows the characteristic "scimitar sacrum."

situated slightly to the left of the midline. Neurological examination indicated hypesthesia in the left second and third sacral segments and relaxation of the anal sphincter. Funduscopic inspection was normal and the routine urine, blood and spinal fluid analyses gave no unusual findings.

Roentgenograms of the lumbosacral spine and coccyx presented the characteristic "scimitar sacrum" associated with anterior meningocele (Fig. 1). There was a large semicircular defect of bone in the left half of the third, fourth, and fifth sacral segments, with a curving deviation of the remaining sacrum and coccyx to the right, and fusion of the coccygeal segments. Pantopaque was then inserted into the lumbar canal and myelograms demonstrated free communication between an extended terminal theca and the large meningocele sac occupying this defect. The communication occurred by means of a pear-shaped pedicle beneath the lamina of the second sacral segment (Figs. 2 and 3).

Operation: February 6, 1945. Operator—M. H. Brown. Anesthesia—spinal (pontocaine 20 mgm.), supplemented terminally with intravenous pentothal.

Transsacral exploration was done through a posterior midline incision extending from the fifth lumbar spine to the coccyx. The aponeurotic attachments of the sacrospinalis and gluteus maximus were incised and retracted, uncovering a bluish, loculated meningocele sac, which measured approximately 5 cm. in diameter and 7 cm. in length to its tapering pedicle beneath the second sacral neural arch. The cyst incompletely filled the dead space formed by the sacral defect, the remaining area containing an excess of fibro-fatty tissue. On the left posterior aspect of the sac was a small dermoid containing sebaceous material. The cyst

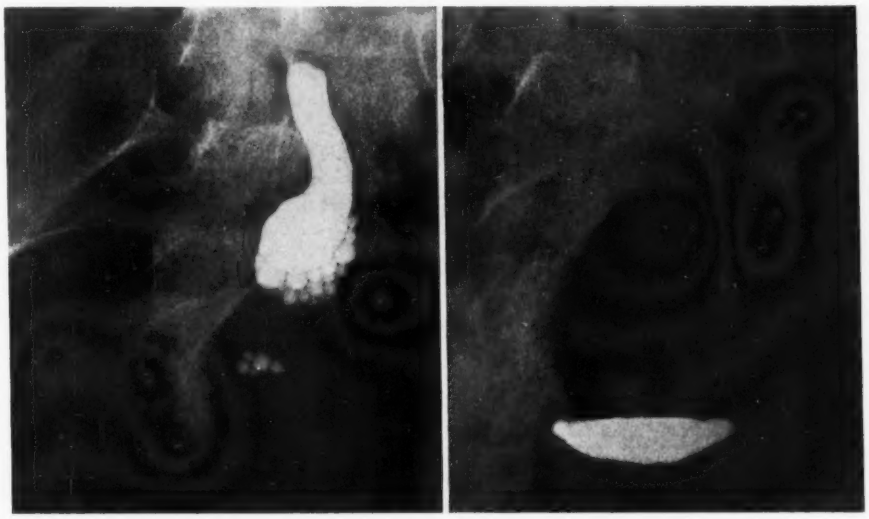

FIG. 2 (*left*). Pantopaque myelogram revealing pear-shaped communication between terminal theca and upper portion of the meningocele sac.

FIG. 3 (*right*). Pantopaque myelogram. The opaque material puddles within the inferior portion of the meningocele sac.

was mobilized and then opened for examination with the patient in Trendelenburg's position. Caudal nerves were identified high on the right posterior wall of the pedicle; no neural elements were incorporated within the sac itself. Following resection of the cyst it was found that the caudal roots could be spared by a slight tenting of the pedicle closure. Accordingly, a double row of interrupted silk sutures, longitudinally directed in the median plane, with interposed muscle strips for reenforcement, were used in plastic closure of the pedicle. A V-shaped flap of dura was employed to form an artificial root pouch on the right. The completed suture line was entirely protected by the bony arch of the second sacral canal. The wound was then closed in layers without drainage.

Course. Chemotherapy was instituted immediately following surgery, employing penicillin (100,000 units) and sulfadiazine (90 gr.) daily for one week. The postoperative course was smooth, the incision healing by primary intention, and, apart from a temperature elevation to 100° on the first postoperative day, entirely afebrile. She voided normally on the day following surgery, and urination subsequently has been normal. The neurological status was unchanged. The patient was kept flat in bed in mild Trendelenburg position until February

25, 1945, when activity was gradually resumed. Recheck pantopaque myelograms then showed a minute leak at the left angle of the suture line into the dead space beneath. This continued until March 20, 1945, with reabsorption of the small amount of spinal fluid occurring within the dead space without external fistula formation. Elastic pressure, employing seasponge, was then applied for two weeks; recheck myelograms on April 1, 1945 demonstrated that the leak had entirely sealed (Fig. 4). In retrospect it was felt that external pressure might have been employed at an earlier date as soon as the danger of incisional necrosis had passed. At the time of discharge on April 6, 1945 the patient was free of headache and sciatica, and incisional tenderness over the sacrum was progressively subsiding. When seen in the Out Patient Clinic early in May she had returned to normal activity and was housekeeping for her family.

FIG. 4. The completed suture line showing slight tenting at the right angle at the site of artificial root pouch formation.

Pathological Report. The sac was a fibrous membrane containing strands of smooth muscle and numerous venous channels. There was an occasional collection of xanthoma cells in the wall. One area showed a surface lining of transitional columnar type epithelium similar to bladder epithelium. In other zones the sac had a distinct squamous epithelial lining and the wall contained sympathetic nerve tissue.

Diagnosis: Meningocele, showing dermoid characteristics and containing sympathetic nerve cells.

SUMMARY

The characteristic clinical and roentgenographic features of anterior sacral meningocele have been noted with a discussion of the operative management of a successfully treated case. The technical aspects of primary excision and closure have been presented with a view to standardizing the surgical treatment of this unusual lesion.

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FULMINATING GAS GANGRENE OF THE BRAIN: REPORT OF A CASE IN A CIVILIAN

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Reports of the effects of infection of the human tissues with Clostridium welchii and associated organisms form a voluminous literature. During the last five (war) years more than three hundred such papers, dealing with all phases of the problem, have been published. Only one report, that by a committee of Soviet scientists,[11] gave consideration to gas infections of the brain. These were complications of craniocerebral injuries acquired in war. The literature contains many accounts of cases of gas gangrene occurring in civilian hospitals, but none with such an infection of the brain. It was therefore thought that report of the following case would be of interest.

CASE REPORT

P. P., a colored male, age 45, was brought to the Accident Room of the Johns Hopkins Hospital in the afternoon of Nov. 11, 1944, with the story of having been struck on the head

FIG. 1. X-ray showing three small depressed fractures in right parietal bone.

with a garden rake about 6 or 7 hours before. There had been no unconsciousness, and the patient complained only of multiple lacerations over the right side of the head. He was ambulatory, and his temperature, pulse and respirations were all normal. About an hour after his admission to the Accident Department he began to show convulsive seizures affecting the left side of his face, and developed a little facial weakness of upper motor neuron type. X-rays at this time revealed three small depressed fractures in the right parietal bone, so spaced that they were quite compatible with the weapon used (Fig. 1).

FIG. 2. Bone fragments have been removed. The subjacent brain is filled with gas bubbles.

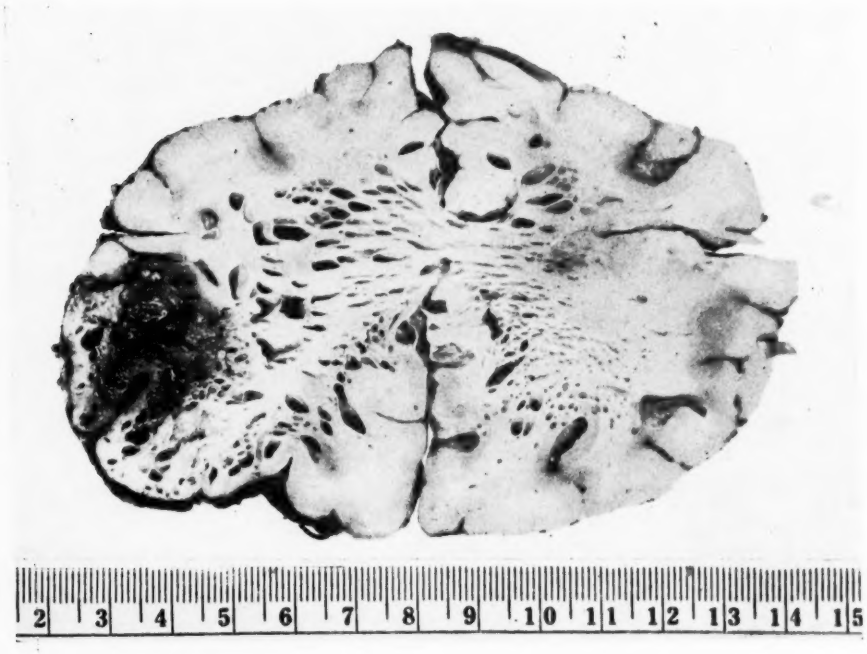

FIG. 3. Cross section of cerebral hemispheres showing necrosis on right and bubbles of gas on both sides.

He was taken to the operating room that evening—about 12 hours after his injury. There, under local novocain anesthesia, the depressed bone fragments were removed from all three fractures. In two of them the dura was torn. Sulfanilamide was placed in the wound after thorough debridement and the wound was closed with silk.

On return to the ward the patient was in good condition, was conscious, alert and able to take fluids. He was given sulfadiazine by mouth prophylactically. About 24 hours after opera-

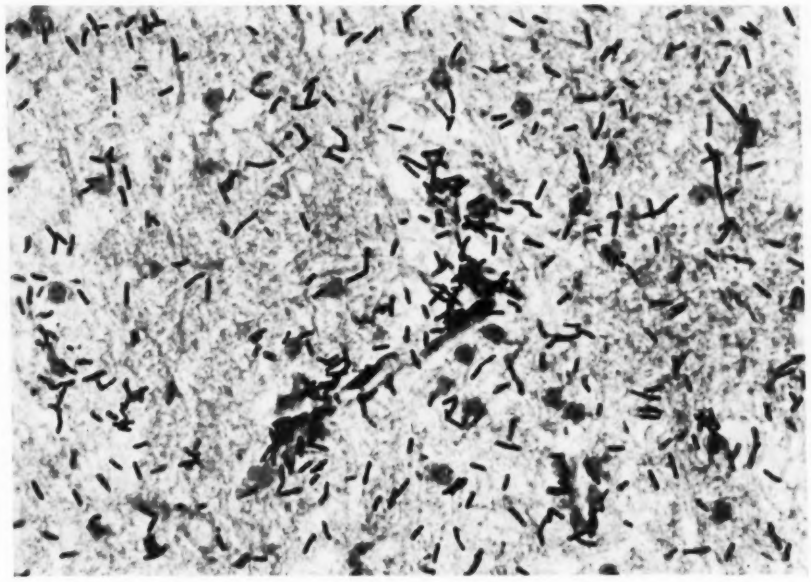

FIG. 4. The brain is loaded with organisms. (×600)

tion the patient's temperature, which had been running from 100° to 101°, suddenly spiked to 103.6°. His wound looked entirely innocent at this time, but the patient was less alert and took fluids poorly. Twelve hours later the temperature was 104.4°. There was some crepitation about the wound and this was opened widely. He was given intravenous fluids, blood, and intramuscular penicillin. Bubbles of gas and necrotic cerebral tissue began to exude from the defect in his scalp and skull. X-rays made at this time revealed honey-combing of the right hemisphere with gas bubbles (Fig. 2). Lumbar puncture revealed grossly cloudy fluid in which numerous Gram-positive rods could be stained. Intrathecal penicillin was begun, he was given anti-gas gangrene antitoxin, but died the following morning, less than 72 hours after his injury, 60 hours after operation. Cultures taken from the wound and of the spinal fluid during life showed massive growth of Clostridium welchii.

At autopsy, performed about four hours later, massive necrosis of the right hemisphere was demonstrated with bubbles of gas over nearly the entire brain (Fig. 3). Clusters of organisms were demonstrated in the tissues (Fig. 4).

COMMENT

Dandy[4] in 1927 reported a case of pneumocephalus of bacterial origin as a sequel to a previous paper on pneumocephalus following trauma.[3] In his case there was a well defined abscess cavity containing gas. A Gram-negative, gas-forming, anaerobic organism was cultured.

This was clearly not Clostridium welchii and could not be accurately identified. He also reviewed one case of Bier[1] and two of Rychlik[8] in which gas-forming organisms (the Welch bacillus) produced cerebral abscesses. The pathological report on the case of Bier is too sketchy to permit formation of any definite conclusions, but it seems clear that the case of Dandy and the two of Rychlik were merely infections by the gas-forming bacilli and were not to be classed with clinical gas gangrene such as occurred in the case being reported.

Qvist[7] emphasized the distinction between gas gangrene, in which there is gas production with necrosis of tissue, and anaerobic cellulitis, where there is active infection by gas-forming anaerobes, but no gangrene. Similar distinctions were also made by Keen,[6] Hosford,[5] and Edwards.[2] Swan[10] states that the term "gas gangrene" should be reserved for those cases showing marked toxemia and massive oedema of tissue as well as the presence of anaerobic gas-forming organisms. These distinctions are important from the point of view of treatment and prognosis in any given case.

It is surprising that more cases of fulminating gas gangrene of the brain have not been described. The report by the Soviet committee[11] states that practically all head injuries were infected. Of 300 cases 11.2 per cent were infected with gas-producing anaerobes (94 per cent Cl. perfringens or welchii). Cl. perfringens was usually found in combination with putrefactive anaerobes, aerobes, and streptococci. The authors describe four forms of anaerobic brain infection, depending upon the clinical course—(1) acute, (2) subacute, (3) chronic, and (4) latent. In the acute form eight out of ten patients died and these clearly had all the criteria necessary for establishment of the diagnosis of "gas gangrene" as proposed in the present report. Their patients had all suffered war wounds, however. Another case, encountered in an American Army Evacuation Hospital, was called to my attention by Sherman.[9] No doubt many more will appear.

In the case presented here two significant points are of interest: First that the weapon inflicting the wound was a garden rake, and secondly, that twelve hours elapsed between the time of injury and debridement of the wound. It suggests that injuries produced by weapons known to be commonly contaminated by the anaerobic organisms should be treated more vigorously in a prophylactic sense than our patient was. No similar infection of the brain appears in the records of the Johns Hopkins Hospital.

SUMMARY

1. A case of gas gangrene of the brain in a civilian is presented together with a brief review of the literature.

2. The fulminating character of the disease in contrast to simple infections by gas-forming organisms is emphasized.

3. The fact that the type of weapon in a civilian injury of the brain is probably of great importance is pointed out.

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CYSTICERCOSIS
A CASE REPORT

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Human infestation with cysticerus cellulosae, the larval stage of Taenia solium—the pork tapeworm—has been a rare recurrence in the United States. It has, however, been encountered frequently in British troops who have served in the Middle East and India where the parasite is common. Inasmuch as many men will be returning to the United States who have been stationed in such areas, the disease may be encountered more frequently. It seems timely, therefore, to report a case of cysticercosis in which the manifest symptoms resulted from involvement of the central nervous system and in which surgical treatment was of benefit.

CASE SUMMARY

A 31-year-old soldier with 2½ years' service was admitted to a general hospital on 6 January 1944 complaining of headaches and difficulty in seeing. He had arrived in Egypt in the summer of 1942. He was well until about 1 November 1942 when, after a severe sandstorm near Benghazi, Libya, he developed a severe headache and blurring of vision. He was admitted to a hospital where he remained for approximately 15 days. Hot applications were used on his eyes, and he was discharged feeling as though he had completely recovered. During the next 11 months he had intermittent headaches. These were not severe, and he performed full duty with an air force service group. In December, 1943 he had chills and fever, and he was told that he had malaria. At this same time his headaches became severe, his vision was blurred, and he developed diplopia on distant gaze. These symptoms persisted until his admission to the hospital on 6 January 1944.

His family history was negative. His past history was noncontributory. He was a native of Louisiana and had lived in New Orleans most of his life.

Examinations. On admission blood pressure was 135/70, temperature 98.6, and pulse 70. The heart and lungs were normal to percussion and auscultation. The abdomen was soft. The spleen and liver were not palpable. The rectal examination was negative. The musculoskeletal system was normal.

Neurological examination revealed bilateral choked discs of 2 diopters. There was a hemorrhage in the right fundus. Vision was: VOD 20/20; VOS 20/20. There was a slight paresis of the right VI cranial nerve. The visual fields were normal. All other cranial nerves were normal. The reflexes were all equally active. The Babinski and Hoffmann signs were negative. There was a slight increase in the release reaction of the right arm. There were no motor or sensory abnormalities. The sedimentation rate (Wintrobe) was 3 mm. in one hour.

RBC = 4,200,000
HBG = 14.5 grams
WBC = 5,000
Diff. (200 cells)
N = 51 L = 40 E = 7 M = 2

No parasites were noted in the blood smear. The urinalysis was negative.

X-ray examination of the skull revealed a marked erosion of the posterior clinoids (Fig. 1). The sella turcica was almost entirely decalcified. The pineal gland was calcified and in normal position. There were two small calcified masses, each measuring about 1×1 mm. One of these lay several cm. posterior to the pineal body and the other high in the parietal lobe (Fig. 1).

X-ray examination of the lungs revealed several small calcified mediastinal areas which were considered to be calcified nodes.

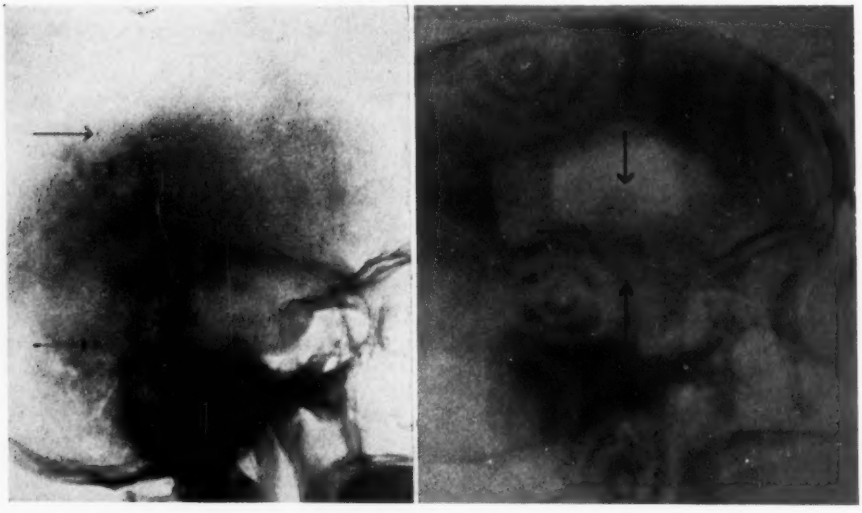

FIG. 1 (*left*). Erosion of the posterior clinoid processes. Arrows indicate two small areas of calcification. Marked decalcification of the sella turcica is present.

FIG. 2 (*right*). Ventriculogram demonstrating slightly enlarged lateral ventricles and cyst outlined by arrows.

On 18 January 1944 a ventriculogram under local procaine anesthesia was carried out. Both lateral ventricles were moderately dilated. The anterior horn of the right ventricle was pushed upward and the third ventricle was compressed posteriorly. A cyst-like mass was noted on the lateral view (Fig. 2), above and slightly posterior to the anterior clinoid process on the right side.

Operation. On 19 January 1944, under gas-oxygen-ether anesthesia administered by the intratracheal route, a right frontal flap was turned down. The dura was incised and the under surface of the right frontal lobe was retracted until the right optic nerve came into view.

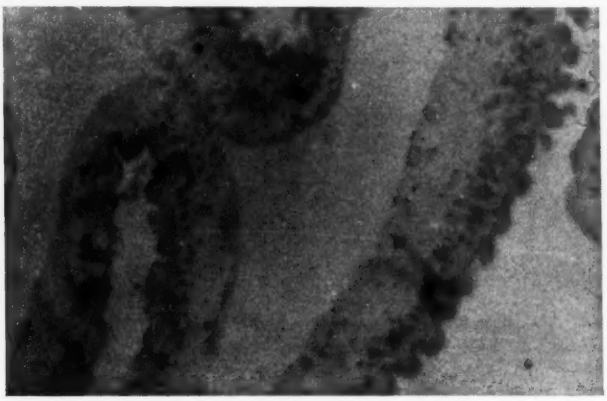

FIG. 3. Cysticercus cellulosae (low power).

Just lateral to it, and seemingly extending posteriorly and inferiorly beneath the right optic tract and the optic chiasm, there was a cyst with a thin, moderately transparent membrane. The membrane was punctured and a large quantity (possibly 1 oz.) of clear, colorless fluid was evacuated. Along with the fluid, numerous small pieces of gelatinous, mucoid material appeared. The largest measured approximately 1×3 cm. The cyst cavity appeared to extend down to the floor of the sella turcica and also a few cm. posteriorly. As much of the cyst wall as could be visualized was removed, and all mucoid material and fluid were sucked out. The dura was closed with silk, the bone flap replaced, and the scalp closed in layers with silk.

Histological Diagnosis: Cysticercus cellulosae (Fig. 3).

Course. X-rays of the extremities and abdomen revealed scattered calcified cysts in the lower extremities (Fig. 4) and several in the abdominal cavity.

His postoperative course was satisfactory. The papilledema disappeared, and on 15 March his general and neurological examinations were negative, and he was returned to limited duty. An encephalogram revealed the lateral ventricles still dilated, but the deformity due to the cyst had disappeared.

He was reexamined in September, 1944, nine months after his operation, as he was returning to the United States on the rotation plan. At this time he stated that he had been doing regular duties with his service group and had felt well. There had been no visual disturbances and no headaches. His companions stated that he had been perfectly normal mentally. On several occasions he had slight vertigo while working in the hot sun during the summer, but this had not bothered him.

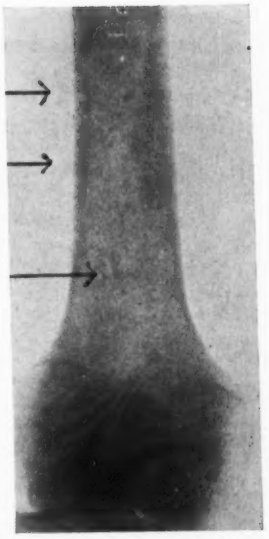

FIG. 4. Lower end of the femur demonstrating calcified larvae.

FIG. 5. Nine months postoperative. There has been a marked recalcification of the sella turcica.

The general and neurological examinations were essentially negative.

X-ray examination revealed complete recalcification of the sella turcica (Fig. 5).

COMMENT

The original infestation in this case probably took place in the United States inasmuch as calcification of other larvae was present at the time of operation, which was only about 18 months after his arrival in Egypt. As a general rule calcification does not occur for from three to six years after infestation.

The diagnosis was not made preoperatively. On review of the x-ray films of the chest the calcified areas noted in the mediastinum are still indistinguishable from calcified nodes.

The patient gave no history of symptoms suggestive of the disease. This is not uncommon as the tissues are quite resistant to live larvae, and it is only after they die that a more intense local reaction occurs. If there are subcutaneous lesions, a common occurrence, the presence of palpable pea-sized nodules together with recovery of the adult worm in the stool makes the diagnosis evident. In their absence, however, diagnosis is difficult until calcification has occurred.

The cyst presenting was associated with the leptomeninges. It was impossible to accomplish the ideal, the removal of all the cyst wall, because of its inaccessibility. Inasmuch as there had been no evidence of recurrence nine months after operation, it is assumed that this particular cyst has been eradicated. When convulsions or other signs of central nervous system disease develop in an adult who has served with the armed forces in the Middle East and India, a diagnosis of cysticercosis must seriously be considered.

SUMMARY

1. A case of cysticercus cellulosae of the brain is presented with surgical removal and with no evidence of recurrence nine months afterward.

2. Inasmuch as many men will be returning from foreign soil where Taenia is prevalent it is important to keep this condition in mind when signs and symptoms of central nervous system disease develop.

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A NEW POSITION FOR FRONTAL CRANIOTOMY*

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Recently in considering the surgical exploration of the circle of Willis for a suspected aneurysm, it seemed worth while to try a new method of approach in the hope of improving

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visibility in the region about the optic chiasm. A head rest was developed (Fig. 1) which securely held the head in such a position that the floor of the anterior fossa was in a horizontal rather than vertical plane. The patient was placed on his abdomen with the neck extended so that the patient's face was toward the surgeon (Fig. 2), much as one would lie on the floor to read with the face held between the hands. The position proved so satisfactory that we have

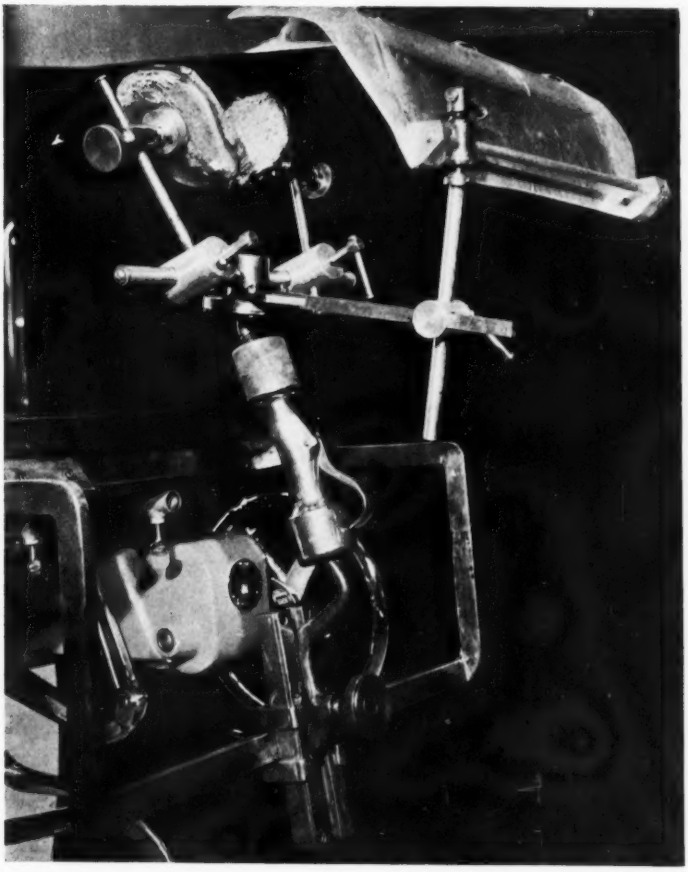

FIG. 1. Head rest attached to operating table. Curved metal shield supports the drapes.

continued to employ it for all operations in the frontal region (Fig. 3). In spite of the unorthodox method of fixation of the head and the hyperextension of the neck, there has been no postoperative complaint of soreness of the face or stiffness of the neck.

The conventional position for transfrontal craniotomy is with the patient's head resting on the occiput with the face up. In spite of the apparent success of this method through the years, it is not difficult to find obvious technical disadvantages that can be improved by altering the position of the patient's head. In the conventional position, as the skin and bone flaps are reflected they must be turned upward and anchored to the drapes. When wrapped in

wound towels, they form a bulky mass which occupies valuable space. It is often difficult to drill the anterior burr holes without striking the handle of the Hudson burr on the drapes.

With the horizontal position, the skin and bone flaps fall forward out of the operative field. Drilling of the anterior burr hole is free from the usual difficulty.

Fig 2. Position of patient, showing method of fixation of head.

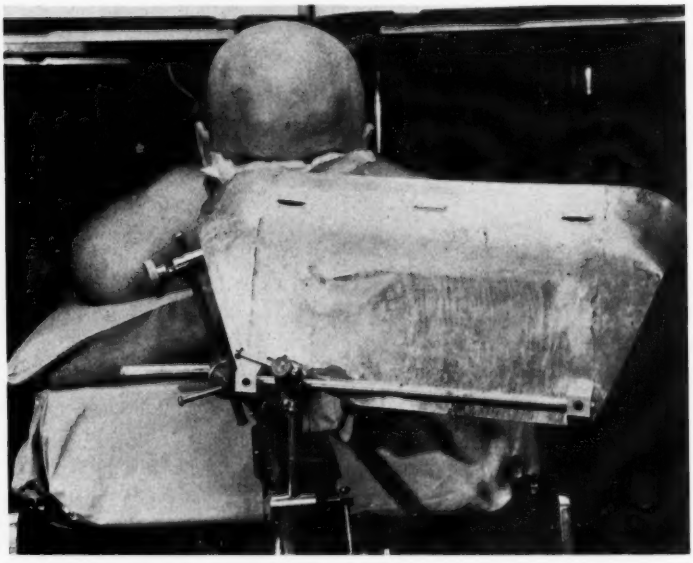

FIG. 3. Patient in position for right transfrontal craniotomy. Adjustable metal shield supports drapes and allows adequate space for anesthetist.

When looking directly down along the vertically placed floor of the anterior fossa visibility about the optic chiasm can only be obtained by considerable retraction of the frontal lobe. The exposure represents a V with proportionately greater exposure at the surface than

at the base. With the head so placed that the floor of the anterior fossa is horizontal, the degree of exposure at the tip of the retractor can be greater than at the surface and still maintain excellent visibility (Fig. 4).

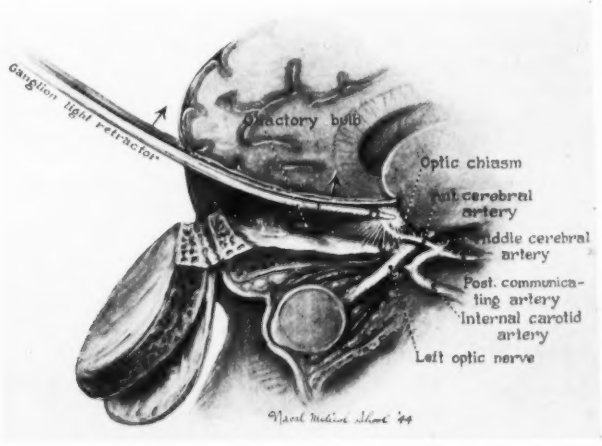

FIG. 4. Illustrates maximum exposure of chiasm without excessive retraction of frontal lobe.

In the usual position, exploration of the posterior portion of the chiasm requires the operator to bend far forward, whereas in the horizontal position, with the table elevated, visibility is directly at eye level (Fig. 5). It also allows the assistants to see equally well and thus be of greater help in the operative procedure.

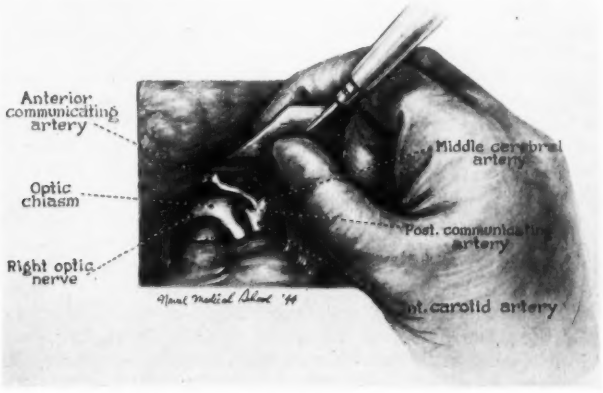

FIG. 5. Drawing made from actual exposure of circle of Willis. Angle of the floor of the anterior fossa allows blood and spinal fluid to gravitate from operative area.

If the head is so fixed that the floor of the anterior fossa slopes slightly forward, all fluid will gravitate from the operative field. Saline for irrigation will run out without the use of suction as will blood which otherwise would accumulate at the bottom of the wound. Even

extensive local hemorrhage will not obstruct visibility such that the bleeding point cannot be located.

Having observed fifty consecutive patients operated upon in this position, it is our impression that the postoperative course is greatly improved. Possibly this reduced reaction is due to the fact that blood does not gravitate into and fill the basal cisterns and subarachnoid space as it must do in the conventional position.

During operation in this position an excessive amount of mucus drains out of the mouth along the intratracheal tube. How much of this passes into the tracheobronchial tree when the patient is lying on his back cannot be determined, but it seems logical that it is better to have it gravitate out along the tube than to rely solely on the use of suction to remove this accumulated secretion.

This position is particularly well suited to the treatment of subdural hematomas and brain abscesses. The drapes can be so arranged that the operative field includes both frontal, temporal and parietal areas. Bilateral exploration can be done without altering the position or redraping the patient's head. Furthermore, drainage of both hematomas and abscesses is aided by gravity.

It is hoped that the use of this position will improve the surgical exposure of the optic chiasm and circle of Willis, as well as aid in the repair of skull defects and exploration of lesions of the orbit and frontal lobe.*

The technical assistance of Mr. John S. Bronson is gratefully acknowledged.

PERIPHERAL NERVE LESION CHARTS

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For the examination and study of peripheral nerve lesions it is important to have simple and accurate outlines of the areas of anaesthesia, high skin resistance, etc. The body charts that have been available for this purpose have a number of serious shortcomings. In the first place they usually show only the front and rear views of the extremities, leaving large blind areas along the lateral and inner surfaces. Second, the positions of the arms and hands are often unnatural and uncomfortable and almost impossible for men with peripheral nerve lesions to hold at all. Third, they do not show any landmarks, without which it is very difficult to transfer the outlines of the affected areas to the chart with any degree of accuracy.

During the past two years, while making skin resistance studies on patients with peripheral nerve lesions at the Walter Reed General and Johns Hopkins Hospitals, we experimented with a number of charts. A series of charts were finally designed which do not have the aforementioned shortcomings.

Fig. 1 shows the chart for the right upper extremity. The central drawings give the front and rear views of the forearm with the forearm flexed at right angles. Most patients with peripheral nerve injuries can easily hold their arm in this position even though they are unable to let their forearms hang freely at the side of the body. This position does not show the posterior and anterior surfaces of the arm, the ulnar and radial surfaces of the forearm, nor the lateral and medial surfaces of the fingers. All of these areas are shown in the drawings at the two sides of the chart in which the forearm hangs freely at the side of the body with the

* The head rest will be available through the American Sterilizer Company, Erie, Pennsylvania.

palmar surface turned toward the body. This is a natural hanging position of the forearm. The drawing at the top and center of the chart shows the axilla and the surrounding region. Thus these charts show every part of the skin on the upper extremity, that is, they do not have any so-called blind areas. The black circles placed over bony prominences aid in copying the pattern of the affected areas. A reverse chart is used for the left upper extremity.

Fig. 2 shows the chart for the lower extremities. The three views at the left give the front, rear and side views of both lower extremities. The half-squatting view at the right shows the inner surfaces of the legs and thighs and the pubic area. At the bottom the center drawings show the plantar surfaces of the feet; the drawings at the sides show enlarged views of the plantar and dorsal surfaces of the toes. These charts do not have any blind areas.

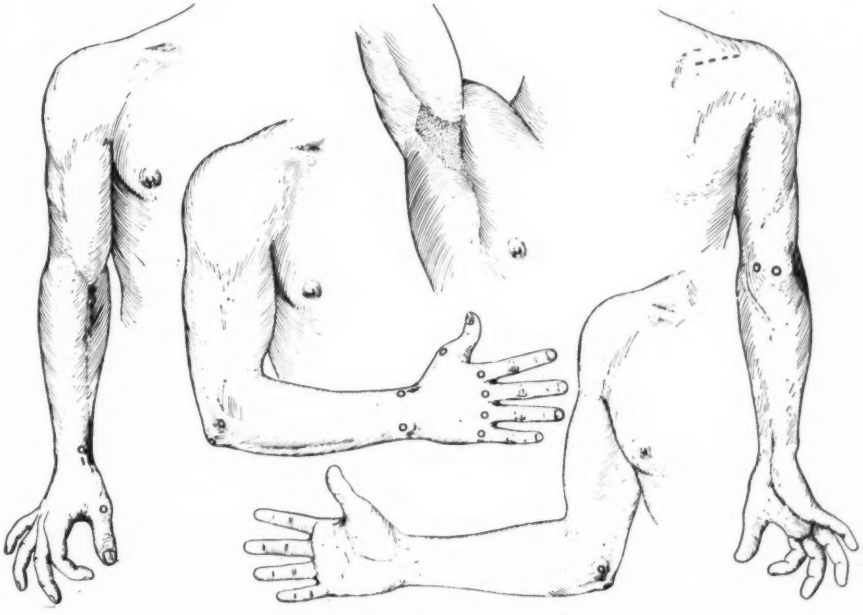

FIG. 1

The charts should be printed in a light red, orange or green rather than in black, since peripheral nerve and other patterns drawn on the charts in pencil, ink or crayon show up much more clearly on charts printed with the colored inks. The orange or red colored charts have the advantage that in photographing they reproduce black.*

These charts can be used not only in mapping areas of anaesthesia and high electrical skin resistance produced by peripheral nerve lesions, but also areas of high electrical skin resistance produced by sympathectomy, spinal cord lesions, paravertebral nerve blocks and areas of anaesthesia produced by intervertebral discs; also for outlining skin grafts or other skin disturbances.

* These charts are printed by The Maryland Press, 402 Fallsway, Baltimore, Maryland.

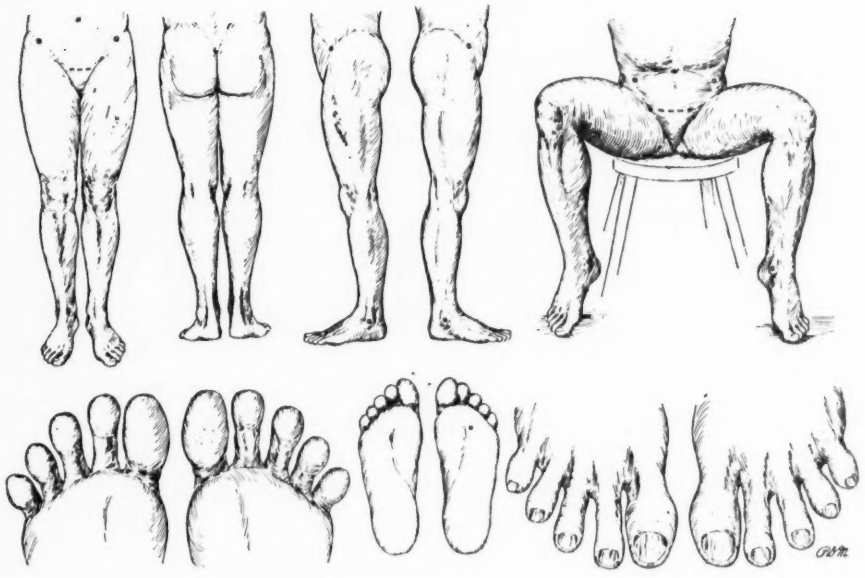

FIG. 2

SUMMARY

Charts are presented which show all parts of the upper and lower extremities for use chiefly in mapping areas of anaesthesia or high electrical skin resistance produced by peripheral nerve and other neurological lesions.

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